PATIENT INFORMATION LEAFLET – PLEGRIDY®

SCHEDULING STATUS S4

PROPRIETARY NAMES, STRENGTH AND DOSAGE FORM

PLEGRIDY 63 µg solution for injection

PLEGRIDY 94 µg solution for injection

PLEGRIDY 125 µg solution for injection

Read all of this leaflet carefully before you start using PLEGRIDY.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- PLEGRIDY has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

1. WHAT PLEGRIDY CONTAINS

The active ingredient is peginterferon beta-1a.

PLEGRIDY 63 µg: Each pre-filled syringe or pen contains 63 microgram peginterferon beta-1a.

PLEGRIDY 94 µg: Each pre-filled syringe or pen contains 94 microgram peginterferon beta-1a.

PLEGRIDY 125 µg: Each pre-filled syringe or pen contains 125 microgram peginterferon beta-1a.

The other ingredients are: Sodium acetate trihydrate, glacial acetic acid, L-arginine hydrochloride, polysorbate 20 and water for injection.

Sugar free.

2. WHAT PLEGRIDY IS USED FOR

The active substance in PLEGRIDY is peginterferon beta-1a. Peginterferon beta-1a is a long-acting form of interferon. Interferons are natural substances made in your body to help protect you from infections and diseases.

PLEGRIDY is used to treat Multiple Sclerosis (MS). PLEGRIDY can help to reduce the number of relapses that you have and slow down the disabling effects of MS. Treatment with PLEGRIDY will not cure MS. Your doctor will advise you for how long you can use PLEGRIDY or when to stop.

MS symptoms also tend to flare up from time to time: this is called a relapse.

3. BEFORE YOU USE PLEGRIDY

Do not use PLEGRIDY

If you are allergic (hypersensitive) to interferon beta, peginterferon beta-1a or any of the other ingredients of PLEGRIDY.

If you are pregnant or are breastfeeding your baby, you should not use PLEGRIDY.

Women who may become pregnant must use reliable contraception.

Take special care with PLEGRIDY:

If you have ever had:

- depression or problems affecting your moods
- thoughts about committing suicide.

Talk to your doctor. Your doctor may still prescribe PLEGRIDY for you, but it's important to let your doctor know if you have had depression or any similar problems affecting your moods in the past.

If there are changes to your mood, for example you have thoughts about suicide; feel unusually sad, anxious or worthless, tell your doctor immediately.

If you know you are allergic or notice any of the following symptoms, **contact a doctor as soon as possible.**

Because PLEGRIDY is based on a protein, allergic reactions may develop.

Signs of an allergic reaction may include:

- becoming wheezy or having difficulty with breathing
- swelling around the face (lips, tongue or throat)
- skin rashes or redness.

If you have any of the conditions listed below, talk to your doctor, pharmacist or nurse before using, especially if they worsen whilst using PLEGRIDY.

- serious liver problems

- irritation at your injection site, which can lead to skin and tissue damage (injection site necrosis). Read carefully and follow the instruction given under ‘How to Inject PLEGRIDY’ to reduce the risk of injection site necrosis.
- a low number of white blood cells or platelets, which can cause an increased risk of infection, bleeding or anaemia
- seizure disorders, not controlled by medication
- heart problems, which can cause symptoms such as chest pain (angina), particularly after any activity; swollen ankles, shortness of breath (congestive heart failure); or an irregular heartbeat (dysrhythmias)
- difficult, laboured breathing or extreme tiredness.

PLEGRIDY may affect your white blood cell counts and your liver function. Your doctor may periodically do a blood test to count the number of white blood cells or platelets and to check that your liver is working properly.

Pregnancy and breastfeeding

The safety and efficacy of PLEGRIDY in pregnancy have not been established. You should not receive treatment with PLEGRIDY if you are pregnant or breastfeeding your baby.

- If you could get pregnant, you need to use contraception while you use PLEGRIDY.
- If you are planning a baby or if you do become pregnant while you are using PLEGRIDY, tell your doctor.

Driving and using machines

No studies on the effects on the ability to drive and use machines have been performed. Patients should determine their individual responses to PLEGRIDY for effects on driving and machine use.

Taking other medicines with PLEGRIDY

Always tell your healthcare professional if you are taking any other medicine.

(This includes complementary or traditional medicines.)

Sometimes you will need to remind other medical staff that you are being treated with PLEGRIDY. For example, if you are prescribed other medicines, or if you have a blood test, PLEGRIDY may affect the other medicines or the test results.

4. HOW TO USE PLEGRIDY

Do not share medicines prescribed for you with any other person.

Always use PLEGRIDY exactly as your doctor has instructed you.

Detailed instructions on how to inject yourself with PLEGRIDY are found in 'How to Inject PLEGRIDY' at the end of this leaflet. You should check with your doctor or pharmacist if you are unsure.

The usual dose for adults 18 years and over

PLEGRIDY is only to be injected once every two weeks.

PLEGRIDY is injected under the skin (subcutaneously). Try to use PLEGRIDY at the same time on the same day every time you inject.

You may experience flu-like symptoms such as headache, muscle aches, chills or fever after injecting PLEGRIDY. These reactions are more frequent when you first start using PLEGRIDY.

Three simple ways may help to reduce the impact of these flu-like symptoms:

1. Use your PLEGRIDY injection just before bedtime. This may allow you to sleep through the effects.
2. Take paracetamol or ibuprofen half an hour before your PLEGRIDY injection and continue taking it for up to a day. Speak to your doctor or pharmacist about a suitable dose.
3. If you have a fever, drink plenty of water to keep you hydrated.

See also "Possible Side Effects, Flu-like symptoms"

Not for Children

PLEGRIDY is not to be used in children below the age of 18 years.

What is in your PLEGRIDY Pack

The PLEGRIDY pre-filled pen Starter Pack holds 2 ready to use pens. Each Starter Pack for PLEGRIDY pen contains a clear, colourless liquid (0,5 ml) containing either 63 or 94 micrograms of peginterferon beta-1a.

The PLEGRIDY pre-filled pen Administration Dose Pack holds 2 or 6 ready to use pens. Each Administration Dose Pack pen contains a clear, colourless liquid (0,5 ml) containing 125 micrograms of peginterferon beta-1a.

Every pen has a pre-attached needle and is ready to inject.

The PLEGRIDY pre-filled syringe Starter Pack holds 2 ready to use syringes. Each Starter Pack for PLEGRIDY syringe contains a clear, colourless liquid (0,5 ml) containing either 63 or 94 micrograms of peginterferon beta-1a.

The PLEGRIDY prefilled syringe Administration Dose Pack holds 2 or 6 ready to use syringes. Each Administration Dose Pack syringe contains a clear, colourless liquid (0,5 ml) containing 125 micrograms of peginterferon beta-1a.

Every syringe has a pre-attached needle and is ready to 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 a Starter Pack containing your first two injections. Read the instructions on how to inject PLEGRIDY before you start using PLEGRIDY.

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

Injecting yourself

You can inject PLEGRIDY yourself without the help of your doctor only if they have trained you to do this. Read and follow the advice given in the instructions on how to inject yourself before you start.

If you have trouble handling the pen or syringe, ask your doctor or nurse 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 immediately. If neither is available, seek help at the nearest hospital or poison control centre.

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, never inject more than once in a 7-day period. Do not use two injections to make up for a missed injection.

If you have problems with your dosing schedule, talk to your doctor.

5. POSSIBLE SIDE EFFECTS

PLEGRIDY can have side effects.

Not all side effects reported for PLEGRIDY are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using PLEGRIDY, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop using PLEGRIDY and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching
- fainting
- yellowing of the skin and eyes, also called jaundice

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to PLEGRIDY. You may need urgent medical attention or hospitalisation.

Frequent side effects:

Changes to levels of liver enzymes

These changes will show up in blood tests. You may not experience any symptoms or you may notice:

- yellowing of your skin or the whites of your eyes (jaundice)
- itching all over
- feeling sick, being sick (nausea and vomiting)
- easy bruising of the skin.

Call a doctor immediately if you do get any of these symptoms. They may be signs of a possible liver problem.

Flu-like Symptoms

Some people find that after injecting PLEGRIDY, they feel like they have mild flu. Signs are:

- headache
- muscle aches
- chills or a fever.

These symptoms are not really flu.

You can’t pass it on to anyone else. They are more frequent when you first start using PLEGRIDY.

Injection site reactions

You may get reactions around the place you inject. Reactions such as redness, itching or pain are frequent.

Swelling, bruising, warmth or rash at the injection site is frequent.

To reduce injection site reactions, read and follow the advice given in the instructions on 'How to inject yourself'.

Other frequent side effects:

- headache
- muscle pain (myalgia)
- pain in your joints, arms, legs or neck (arthralgia)
- chills, feeling cold
- feeling weak and tired (asthenia)
- feeling or being sick (nausea or vomiting)
- itchy skin (pruritus)
- increase in body temperature

If any of the effects trouble you, talk to your doctor.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF PLEGRIDY

How to store PLEGRIDY

Store PLEGRIDY in the refrigerator (between 2 °C and 8 °C).

Do not freeze PLEGRIDY. If PLEGRIDY is frozen, you must discard the syringes/pens.

Keep PLEGRIDY syringes/pens in the closed original carton to protect from light until you are ready to use the injection.

Once removed from the refrigerator, allow PLEGRIDY to warm to room temperature (about 30 minutes) prior to injection. Do not use external heat sources such as hot water to warm PLEGRIDY.

KEEP THIS MEDICINE OUT OF REACH OF CHILDREN.

Do not use after the expiry date stated on the carton. The expiry refers to the last day of the month.

If a refrigerator is not available, PLEGRIDY can be left at room temperature 2 °C to 25 °C, for up to 30 days. Keep the outer carton closed to protect PLEGRIDY from light. If you are unsure whether PLEGRIDY has been stored at room temperature for 30 days or more, you must discard it.

PLEGRIDY does not contain preservatives.

Do NOT use PLEGRIDY if you notice any of the following:

- If the pre-filled pen/syringe is broken.
- If the solution is coloured or you can see particles floating in it.

Disposal

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

7. PRESENTATION OF PLEGRIDY

Pre-filled Syringe:

Each unit of PLEGRIDY is stored in a 1 ml Type I clear colourless glass syringe with a latex free grey bromobutyl rubber stopper and thermoplastic and polypropylene rigid needle shield. A 29 gauge, 1,27 cm staked needle is pre-affixed to the syringe. A single pre-filled syringe contains 0,5 ml of solution of PLEGRIDY containing either 63 micrograms, 94 micrograms, or 125 micrograms of peginterferon beta-1a.

Pre-filled Pen:

Each unit of PLEGRIDY is stored in a 1 ml Type I clear colourless glass syringe with a latex free grey bromobutyl rubber stopper and thermoplastic and polypropylene rigid needle shield. A 29 gauge, 1,27 cm staked needle is pre-affixed to the syringe. A single pre-filled syringe contains 0,5 ml of solution of PLEGRIDY containing either 63 micrograms, 94 micrograms, or 125 micrograms of peginterferon beta-1a. The glass syringe is contained within a single-use, disposable, injection device (pre-filled pen).

Pack sizes:

Pack size 1: Starter Pack containing 1 x PLEGRIDY 63 µg and 1 x PLEGRIDY 94 µg

Pack size 2: 2 x PLEGRIDY 125 µg

Pack size 3: 6 x PLEGRIDY 125 µg

8. IDENTIFICATION OF THE MEDICINE

Sterile, clear, colourless liquid essentially free of visible particles.

9. REGISTRATION NUMBERS

PLEGRIDY 63 µg: 48/32.16/0426

PLEGRIDY 94 µg: 48/32.16/0427

PLEGRIDY 125 µg: 48/32.16/0428

10. NAME AND THE BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE

Acino Pharma (Pty) Ltd

106 16th Road

Midrand, Gauteng, 1686

South Africa

11. DATE OF PUBLICATION OF THE PATIENT INFORMATION LEAFLET

Date of registration: 27 November 2017

How to inject PLEGRIDY

PLEGRIDY Pre-filled syringe

Before you start

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

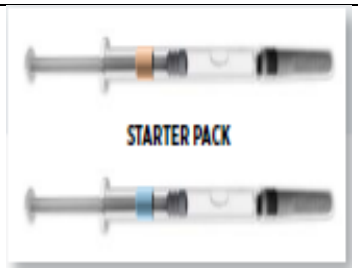
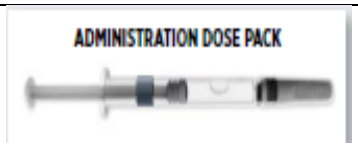
Storage

Once removed from the refrigerator, allow PLEGRIDY to warm to room temperature (about 30 minutes) prior to injection. Do not use external heat sources such as hot water to warm.

If PLEGRIDY is at room temperature for a total of 30 days, it should be used or discarded. If it is not clear if PLEGRIDY has been stored at room temperature 30 days or more, it should be discarded.

DOSE SCHEDULE

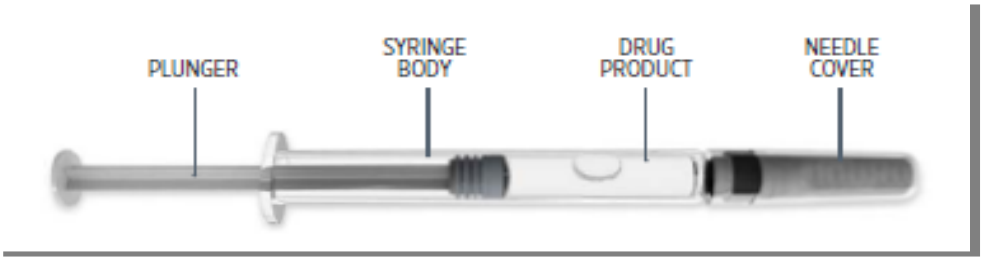
Choose the correct PLEGRIDY pre-filled syringe from a pack. PLEGRIDY pre-filled syringe Starter Pack contains your first two injections to gradually adjust your dose.

WHEN	WHICH DOSE	WHICH PACK
Day 1 (63 micrograms)	First injection: 63 micrograms, choose orange labelled syringe	
Day 14 (94 micrograms)	Second injection: 94 micrograms, choose blue labelled syringe	
Day 28 and then every 2 weeks after (125 micrograms)	Full dose injection: 125 micrograms, choose grey labelled syringe	

Do not *use more than one pre-filled syringe per 14-day period (every 2 weeks).*

PREPARING FOR INJECTION

KNOW THE PRE-FILLED SYRINGE FEATURES



PREPARE WORK SURFACE

Find a well-lit, clean, flat surface like a table and collect all the supplies you will need to give yourself or to receive an injection.

Collect supplies. You will need the following supplies to perform the injection:

- Alcohol wipe
- Gauze pad
- Adhesive bandage/Plaster
- A puncture resistant container for disposal of used syringes

REMOVE FROM REFRIGERATOR

Remove 1 PLEGRIDY Pack out of the refrigerator and select the appropriate pre-filled syringe (dosage) from the pack.

If using the Starter Pack, close the pack and put back in the refrigerator after removal of the first injection pre-filled syringe.

CHECK THE PACK AND THE PRE-FILLED SYRINGE

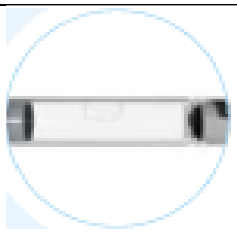
Check the expiration date printed on the PLEGRIDY prefilled syringe, and the outer carton.

Do not use the PLEGRIDY pre-filled syringe past the expiration date.

Let the pre-filled syringe sit for 30 minutes before injecting the PLEGRIDY dose to allow the medication to reach room temperature.

Do not use external heat sources such as hot water to warm the PLEGRIDY pre-filled syringe.

Check that the medication is clear and colourless	

Do not use PLEGRIDY pre-filled syringe if the liquid is coloured, cloudy, or contains floating particles.	

GIVING THE INJECTION

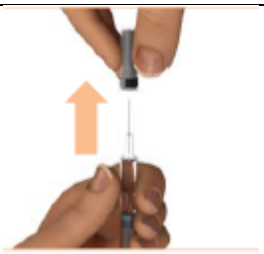
PLEGRIDY pre-filled syringe is for subcutaneous injection.

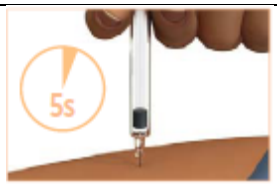
Inject the PLEGRIDY pre-filled syringe exactly as your healthcare provider has shown you.

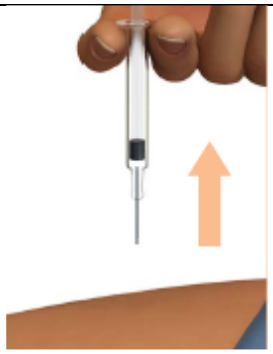
Do not inject into an area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way.

Do not remove the Needle Cover until ready to inject.

Wash your hands with soap and water.

1. CHOOSE THE INJECTION SITE	
Choose an injection site and wipe the skin with an alcohol wipe. Let the injection site dry before injecting the dose. PLEGRIDY pre-filled syringe should be injected into the thigh, abdomen or upper arm. Do not touch this area again before giving the injection.	
2. FIRMLY REMOVE NEEDLE COVER	
Pull the Needle Cover straight off the needle and dispose of the Needle Cover. Do not touch the needle. Do not recap the PLEGRIDY pre-filled syringe.	
3. PREPARE INJECTION SITE AND POSITION PRE-FILLED SYRINGE	

Pinch the skin around the cleaned injection site using thumb and forefinger. Hold the PLEGRIDY syringe at a 90° angle to the injection site.	
4. INJECT MEDICATION	
Quickly insert the needle straight into the skin fold until the needle is fully under the skin. The skin fold can be released after needle insertion.	
Slowly push the Plunger in one smooth motion until syringe is empty. This should take about 5 seconds. Do not lift the pre-filled syringe off the injection site.	
5. WAIT 5 SECONDS	
Keep the needle inserted for 5 seconds.	
6. REMOVE PRE-FILLED SYRINGE FROM SITE	

Pull the needle straight out. Do not recap the PLEGRIDY pre-filled syringe. Do not reuse the PLEGRIDY pre-filled syringe.	

AFTER THE INJECTION

CARE FOR INJECTION SITE

Apply pressure to the injection site for a few seconds using a sterile gauze pad.

If there is blood, wipe it off.

Apply an adhesive bandage if needed.

DISPOSE OF PRE-FILLED SYRINGE

Throw away the used PLEGRIDY pre-filled syringe in a sharps container or some type of hard plastic or metal container with a screw cap such as a detergent bottle or coffee can.

Check with your healthcare provider about the right way to throw away the container.

There may be local or state laws about how to throw away used PLEGRIDY pre-filled syringes.

Do not throw away used PLEGRIDY pre-filled syringe in household trash or recycling bins.

RECORD DATE AND LOCATION

Record the date and location of each injection and alternate sites between your injections.

Do not use the same injection site for consecutive injections.

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 or nurse.

PLEGRIDY Pre-filled pen

BEFORE YOU START

Read the Instructions for Use before you start using PLEGRIDY and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

STORAGE

Once removed from the refrigerator, allow PLEGRIDY to warm to room temperature (about 30 minutes) prior to injection. Do not use external heat sources such as hot water to warm.

DOSE SCHEDULE

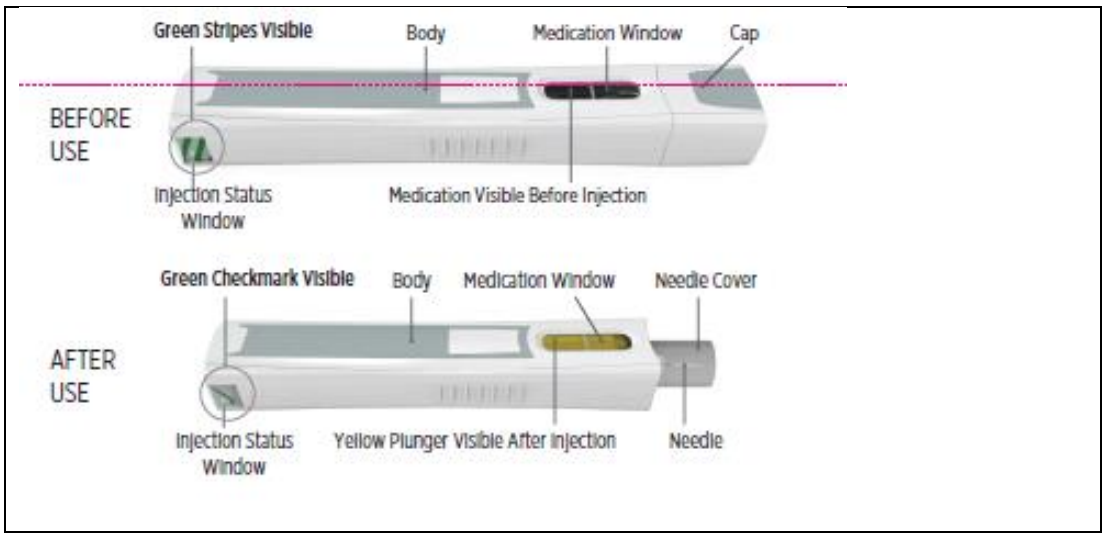
Choose the correct PLEGRIDY Pen from a pack. PLEGRIDY pre-filled pen Starter Pack contains your first two injections to gradually adjust your dose.

WHEN	WHICH DOSE	WHICH PACK
Day 1 (63 micrograms)	First injection: 63 micrograms, choose orange pen	
Day 14 (94 micrograms)	Second injection: 94 micrograms, choose blue pen	
Day 28 and then every 2 weeks after (125 micrograms)	Full dose injection: 125 micrograms, choose grey pen	

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

PREPARING FOR INJECTION

KNOW THE PEN FEATURES



PREPARE WORK SURFACE

Find a well-lit, clean, flat surface like a table and collect all the supplies you will need to give yourself or to receive an injection.

Collect supplies. You will need the following supplies to perform the injection:

- Alcohol wipe
- Gauze pad
- Adhesive bandage
- A puncture resistant container for disposal of used pens

REMOVE FROM REFRIGERATOR

Remove 1 PLEGRIDY Pack out of the refrigerator and select the appropriate pen (dosage) from the pack.

If using the Starter Pack, close the pack and put back in the refrigerator after removal of the first injection prefilled pen.

CHECK PACK AND PEN

Check the expiration date printed on the PLEGRIDY Pen, PLEGRIDY Pen carton, and the outer carton. Do not use the PLEGRIDY Pen past the expiration date.

Check injection status. Make sure that green stripes are visible. Do not use the pen unless injection status window shows green stripes	

Let the pen sit for 30 minutes before injecting the PLEGRIDY dose to allow the medication to reach room temperature.

Do not use external heat sources such as hot water to warm the PLEGRIDY Pen.

Check that the medication is clear and colourless in the medication window.

Do not use the PLEGRIDY Pen if the liquid is coloured, cloudy, or contains floating particles.



GIVING THE INJECTION

PLEGRIDY Pen is for subcutaneous injection.

Inject the PLEGRIDY Pen exactly as your healthcare provider has shown you.

Do not inject into an area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way.

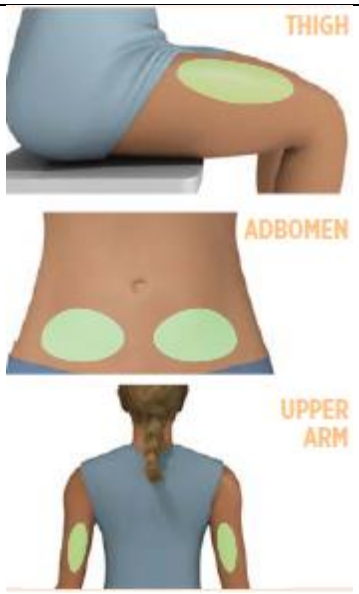
Do not remove the cap until ready to inject.

Wash your hands with soap and water.

<table>
<tr><td colspan="2">1. CHOOSE THE INJECTION SITE</td></tr>
<tr><td>Choose an injection site and wipe the skin with an alcohol wipe.

Let the injection site dry before injecting the dose.

PLEGRIDY Pen should be injected into the thigh, abdomen or upper arm.

Do not touch this area again before giving the injection.</td><td>
</td></tr>
<tr><td colspan="2">2. REMOVE CAP</td></tr>
<tr><td>Pull the Cap off and dispose of the Cap.

The needle is covered by the needle guard and will not be visible.</td><td></td></tr>
<tr><td colspan="2">3. POSITION PEN AND CHECK</td></tr>
<tr><td>Position the PLEGRIDY Pen so that the green stripes are visible.

Do not use the pen unless injection status window shows green stripes.</td><td></td></tr>
</table>

Hold the PLEGRIDY Pen at a 90° angle to the injection site.	
4. INJECT MEDICATION	
Press into site and hold until clicking stops and green checkmarks appear. Pressing down will insert the needle and automatically start the injection. Do not lift the pen off the injection site. Do not make any movements until injection is completed. Continue to firmly press down, hold the Pen at a 90° angle and keep your hand steady until the injection is completed.	
During the injection process: PLEGRIDY Pen will “click” several times. Green stripes pattern will be moving in the injection status window. The pen’s clicking sounds will stop when the injection is complete.	
Check for completion. Make sure the green check marks have appeared in the injection status window.	
5. REMOVE PEN FROM SITE	

Lift the PLEGRIDY Pen from the injection site. The needle guard will extend covering the needle completely.	

AFTER THE INJECTION

CARE FOR INJECTION SITE

Apply pressure to the injection site for a few seconds using a sterile gauze pad.

If there is blood, wipe it off.

Apply an adhesive bandage if needed.

VERIFY DOSE DELIVERY

Check that the yellow plunger extends through the Medication Window.



An extended yellow plunger indicates that the entire dose has been successfully administered.

Do not reuse the PLEGRIDY Pen.

DISPOSE OF PEN

Throw away the used PLEGRIDY Pen in a sharps container or some type of hard plastic or metal container with a screw cap such as a detergent bottle or coffee can.

Check with your healthcare provider about the right way to throw away the container.

There may be local or state laws about how to throw away used Pens.

Do not throw away used PLEGRIDY Pen in household trash or recycling bins.

RECORD DATE AND LOCATION

Record the date and location of each injection and alternate sites between your injections.

Do not use the same injection site for consecutive injections.

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 or nurse.