PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ZIEXTENZO (6 mg, solution for injection in pre-filled syringe)

Pegfilgrastim

Contains 30 mg sorbitol per pre-filled syringe

Read all of this leaflet carefully before you are given ZIEXTENZO

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- ZIEXTENZO 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.

WHAT IS IN THIS LEAFLET

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

1. WHAT ZIEXTENZO IS AND WHAT IT IS USED FOR

ZIEXTENZO contains the active substance pegfilgrastim. Pegfilgrastim is a protein produced by biotechnology in bacteria called *E. coli*. It belongs to a group of proteins called cytokines and is very similar to a natural protein (granulocyte-colony stimulating factor) produced by your own body.

ZIEXTENZO is used to reduce the duration of neutropenia (low white blood cell count) and the occurrence of febrile neutropenia (low white blood cell count with a fever) which can be caused by the use of cytotoxic chemotherapy (medicines that destroy rapidly growing cells). White blood cells are important as they help your body fight infection. These cells are very sensitive to the effects of chemotherapy which can cause the number of these cells in your body to decrease. If white blood cells fall to a low level, there may not be enough left in the body to fight bacteria and you may have an increased risk of infection.

Your doctor has given you ZIEXTENZO to encourage your bone marrow (part of the bone which makes blood cells) to produce more white blood cells that help your body fight infection.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE ZIEXTENZO

Do not use ZIEXTENZO:

- If you are hypersensitive (allergic) to pegfilgrastim, filgrastim, *E. coli* derived proteins, or any of the other ingredients of ZIEXTENZO (listed in section 6).

Warnings and precautions

Tell your doctor or health care provider before using ZIEXTENZO:

- if you experience an allergic reaction including weakness, drop in blood pressure, difficulty breathing, swelling of the face (anaphylaxis), redness and flushing, skin rash and areas of the skin that itch.
- if you experience a cough, fever and difficulty breathing. This can be a sign of Acute Respiratory Distress Syndrome (ARDS).
- if you have any of the following or combination of the following side effects:
    - swelling or puffiness, which may be associated with passing water less frequently, difficulty breathing, abdominal swelling and feeling of fullness, and a general feeling of tiredness

  - These could be symptoms of condition called “Capillary Leak Syndrome” which causes blood to leak from the small blood vessels into your body (see section 4).
- if you get left upper abdominal pain or pain at the tip of your shoulder. This may be a sign of a problem with your spleen (splenomegaly).
- if you have recently had a serious lung infection (pneumonia), fluid in the lungs (pulmonary oedema), inflammation of the lungs (interstitial lung disease) or an abnormal chest x-ray (lung infiltration).
- if you are aware of any altered blood cell counts (e.g. increase in white blood cells or anaemia) or decreased blood platelet counts, which reduces the ability of your blood to clot (thrombocytopenia). Your doctor may want to monitor you more closely.
- if you have sickle cell anaemia. Your doctor may monitor your condition more closely.
- if you are a patient with breast cancer or lung cancer, ZIEXTENZO in combination with chemotherapy and/or radiation therapy may increase your risk of a pre-cancerous blood condition called myelodysplastic syndrome (MDS) or a blood cancer called acute myeloid leukaemia (AML). Symptoms may include tiredness, fever, and easy bruising or bleeding.
- if you have sudden signs of allergy such as rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or trouble breathing these could be signs of a severe allergic reaction.
- inflammation of the aorta (the large blood vessel which transports blood from the heart to the body) has been reported rarely in cancer patients and healthy donors. The symptoms can include fever, abdominal pain, malaise, back pain and increased inflammatory markers. Tell your doctor if you experience these symptoms.

Your doctor will check your blood and urine regularly as pegfilgrastim can harm the tiny filters inside your kidneys (glomerulonephritis).

Severe skin reactions (Stevens-Johnson syndrome) have been reported with the use of ZIEXTENZO. Stop using ZIEXTENZO and seek medical attention immediately if you notice any of the symptoms described in section 4.

You should talk to your doctor about your risks of developing cancers of the blood. If you develop or are likely to develop cancers of the blood, you should not use ZIEXTENZO, unless instructed by your doctor.

Loss of response to pegfilgrastim

If you experience a loss of response or failure to maintain a response with pegfilgrastim treatment, your doctor will investigate the reasons why, including whether you have developed antibodies which neutralise pegfilgrastim's activity.

Other medicines and ZIEXTENZO

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines) .

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

Driving and using machines

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

ZIEXTENZO contains sorbitol and sodium

ZIEXTENZO contains 30 mg sorbitol in each pre-filled syringe which is equivalent to 50 mg/m.
ZIEXTENZO contains less than 1 mmol (23 mg) sodium per 6 mg dose, that is to say essentially 'sodium-free'.

3. HOW TO USE ZIEXTENZO

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

Always use ZIEXTENZO exactly as your doctor has told you. Check with your doctor if you are not sure.

ZIEXTENZO is for use in adults aged 18 and over.

The usual dose is one 6 mg subcutaneous injection (injection under your skin) using a pre-filled syringe and it should be given at least 24 hours after your last dose of chemotherapy at the end of each chemotherapy cycle.

Injecting ZIEXTENZO yourself

Your doctor may decide that it would be more convenient for you to inject ZIEXTENZO yourself. Your doctor or nurse will show you how to inject yourself. Do not try to inject yourself if you have not been trained.

For further instructions on how to inject yourself with ZIEXTENZO, please read the section at the end of this leaflet.

Do not shake ZIEXTENZO vigorously as this may affect its activity.

If you use more ZIEXTENZO than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to inject ZIEXTENZO

If you are injecting yourself and have forgotten your dose of ZIEXTENZO, you should contact your doctor to discuss when you should inject the next dose.

Do not take a double dose to make up for forgotten individual doses.

4. POSSIBLE SIDE EFFECTS

ZIEXTENZO can have side effects.

Not all side effects reported for ZIEXTENZO are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving ZIEXTENZO, please consult your health care provider for advice.

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

- Swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing.
- Spleen rupture. Some cases of splenic rupture were fatal. It is important that you contact your doctor immediately if you experience pain in the upper left side of the abdomen or left shoulder pain since this may relate to a problem with your spleen.
- Stevens-Johnson syndrome, which can appear as reddish target-like or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flulike symptoms.
- Swelling or puffiness, which may be associated with passing water less frequently, difficulty breathing, abdominal swelling and feeling of fullness, and a general feeling of tiredness. These symptoms generally develop in a rapid fashion. These could be symptoms of a less frequent condition called “Capillary Leak Syndrome” which causes blood to leak from the small blood vessels into your body and needs urgent medical attention.

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

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Increased spleen size.
- Bleeding from the lung (pulmonary haemorrhage).
- Breathing problems. If you have a cough, fever and difficulty breathing please tell your doctor.
- Coughing up blood (haemoptysis).
- Damage to the tiny filters inside your kidneys (glomerulonephritis).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following

Frequent side effects:

- Low platelet count (symptoms include bleeding or bruising more easily than normal).
- Lack of white blood cells (symptoms include frequent infections such as fever, severe chills, sore throat or mouth ulcers).
- Headache.
- Nausea.
- Skin rash.
- General aches and pains in the bone, joints and muscles.
- Pain or redness at the site of injection.
- Chest pain.

Less frequent side effects:

- Inflammation of the aorta (the large blood vessel which transports blood from the heart to the body).
- Sweet's syndrome (plum-coloured, raised, painful lesions on the limbs and sometimes the face and neck with fever) has occurred but other factors may play a role.

- Cutaneous vasculitis (inflammation of the blood vessels in the skin).
- Redness at the site of injection.
- Some changes may occur in your blood, but these will be detected by routine blood tests.
- Blood disorders (myelodysplastic syndrome [MDS] or acute myeloid leukaemia [AML]).

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

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of ZIEXTENZO.

Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

5. HOW TO STORE ZIEXTENZO

- Do not use this medicine after the expiry date, which is stated on the carton and on the syringe label after EXP. The expiry date refers to the last day of that month.
- Store in a refrigerator (2 °C - 8 °C).
- You may take Ziextenzo out of the refrigerator and keep it at room temperature (not above 35 °C) for no longer than 120 hours. Once a syringe has been removed from the refrigerator and has reached room temperature (not above 35 °C) it must either be used within 120 hours or disposed of.
- Do not freeze. Ziextenzo may be used if it is accidentally frozen for a single period of less than 24 hours.
- Keep the container in the outer carton in order to protect from light.
- Do not use this medicine if you notice it is cloudy or there are particles in it.

- **STORE ALL MEDICINES OUT OF REACH OF CHILDREN.**

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What ZIEXTENZO contains:

The active substance is pegfilgrastim. Each pre-filled syringe contains 6 mg of pegfilgrastim in 0 ,6 ml of solution.

The other ingredients are:

Acetic acid, polysorbate 20, sorbitol, sodium hydroxide (for pH adjustment), water for injection.

What ZIEXTENZO looks like and contents of the pack

Ziextenzo is a colourless to slightly yellowish solution for injection in a pre-filled syringe (6 mg/0,6 ml).

Pack sizes:

Each pack contains 1 glass pre-filled syringe with a rubber plunger stopper, a plunger rod, an attached stainless-steel needle and needle cap. The syringes are provided with an automatic needle guard.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Sandoz SA (Pty) Ltd[1]

Waterfall 5-lr

Magwa Crescent West

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Jukskei View

2090

This leaflet was last revised in

07 March 2023

Registration number

55/8.5/0736

Access to the corresponding Professional Information

Not applicable

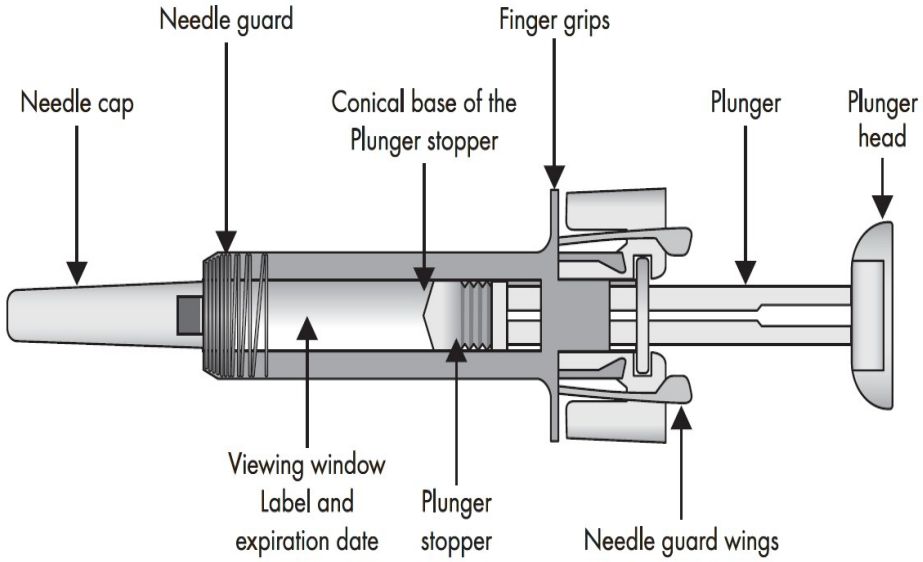
[1]Company Reg. No.: 1990/001979/07

Instructions for use of ZIEXTENZO pre-filled syringe

To help avoid possible infections and to ensure that you use the medicine correctly, it is important that you follow these instructions.

Read ALL the way through these instructions before injecting. It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. The carton contains the pre-filled syringe individually sealed in a plastic blister.

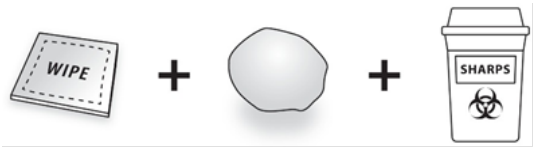
Your ZIEXTENZO pre-filled syringe with needle guard



After the medicine has been injected, the needle guard will be activated to cover the needle. The needle guard is intended to protect healthcare professionals, caregivers and patients from accidental needle sticks after the injection.

What you additionally need for your injection:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.



Important safety information
Caution: Keep the pre-filled syringe out of the sight and reach of children.

- Do not open the carton until you are ready to use the pre-filled syringe.
- Do not use the pre-filled syringe if the seal of the blister is broken, as it may not be safe for you to use.
- Never leave the pre-filled syringe unattended where others might tamper with it.
- Do not shake the pre-filled syringe.

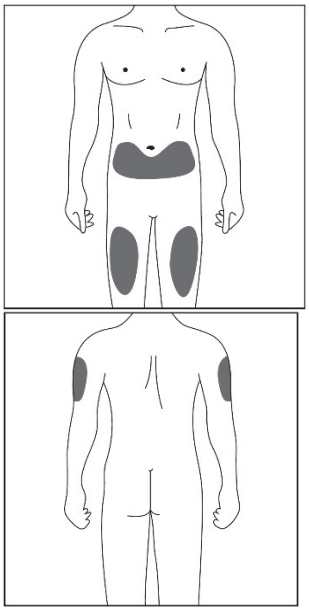
- Be careful not to touch the needle guard wings before use. By touching them, the needle guard may be activated too early.
- Do not remove the needle cap until just before you give the injection.
- The pre-filled syringe cannot be re-used. Dispose of the used pre-filled syringe immediately after use in a sharps container.

Storage of the ZIEXTENZO pre-filled syringe

1. Store the blistered pre-filled syringe in its carton to protect it from light.
2. Store in the refrigerator between 2 °C and 8 °C. **Do not freeze**.
3. Prior to use, remove the pre-filled syringe from the refrigerator and allow Ziextenzo to reach room temperature (up to a maximum of 35 °C) for approximately 15-30 minutes.

4. **Do not use** the pre-filled syringe after the expiry date which is stated on the carton or syringe label. If it has expired, return the entire pack to the pharmacy.

The injection site



The injection site is the place on the body where you are going to use the pre-filled syringe.

- The recommended site is the front of your thighs. You may also use the lower abdomen, but **not** the area 5 cm around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

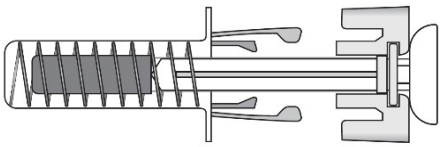
If a caregiver is giving you the injection, the outer upper arms may also be used.

Preparing the ZIEXTENZO pre-filled syringe ready for use

- Take the carton containing the blistered pre-filled syringe out of the refrigerator and leave it **unopened** for approximately 15-30 minutes so that it reaches room temperature.
- When you are ready to use the pre-filled syringe, open the blister and wash your hands thoroughly with soap and water.
- Clean the injection site with an alcohol swab.
- Remove the pre-filled syringe from the blister. Check to ensure the plastic transparent needle guard is situated over the barrel of the glass syringe. If the transparent needle guard is covering the needle cap (as shown below) the syringe has been activated, DO NOT use this syringe and take a new syringe. The figure below shows a ready to use syringe.
- Inspect the pre-filled syringe. The liquid should be clear. Its colour may vary from colourless to slightly yellowish. You may see a small air bubble in the liquid. This is normal. **Do not use** the pre-filled syringe if any other particulates and/or discolouration are observed.

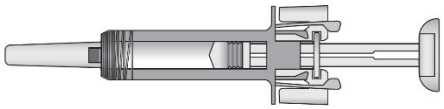
- **Do not use** if the syringe is broken or activated. Return the Ziextenzo pre-filled syringe and the package to your pharmacy.

Device ACTIVATED – DO NOT USE



In this configuration the needle guard is ACTIVATED – DO NOT USE the pre-filled syringe

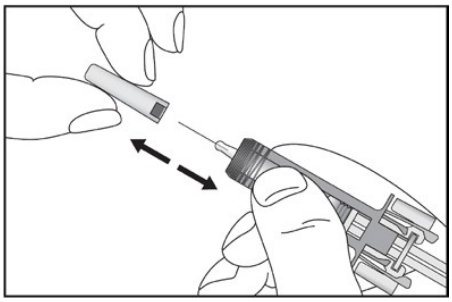
Device READY TO BE USED



In this configuration the needle guard is NOT ACTIVATED and the pre-filled syringe is ready for use

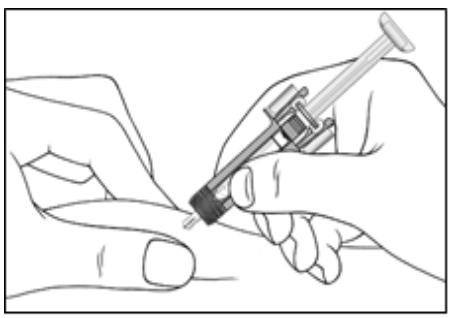
How to use the ZIEXTENZO pre-filled syringe

1.

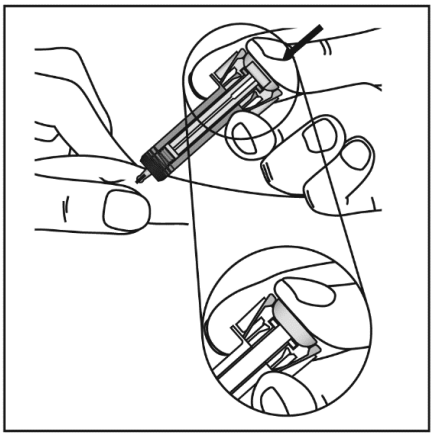


Carefully pull the needle cap straight off. You may see a drop of liquid at the end of the needle. This is normal.

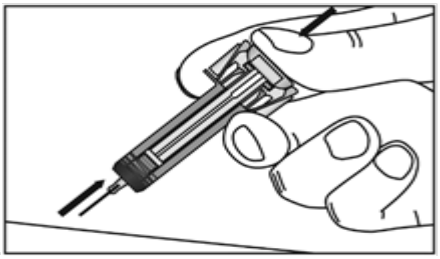
2.



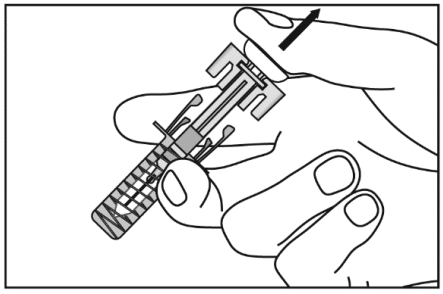
Gently pinch the skin at the injection site and insert the needle as shown. Push the needle all the way in to ensure that fully administered.

3. 

Holding the pre-filled syringe as shown, slowly depress the plunger as far as it will go so that the plunger head is completely between the needle guard wings.
Keep the plunger pressed fully down while you hold the syringe in place for 5 seconds.

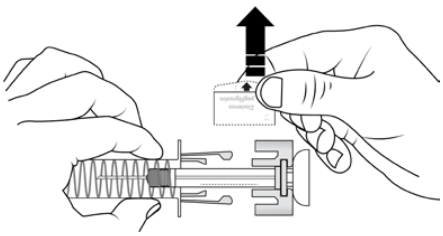
4. 

Keep the plunger fully depressed while you carefully pull the needle straight out from the injection site and let it go off your skin.

5. 

Slowly release the plunger and allow the syringe needle guard to automatically cover the exposed needle.
There may be a small amount of blood at the injection site. You can press a cotton ball or gauze onto the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

6.

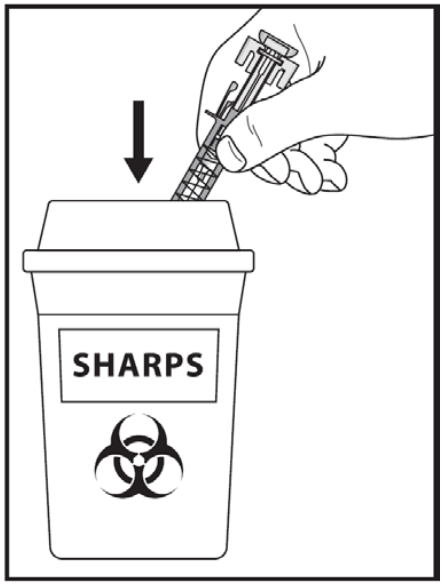


Healthcare providers only

The trade name of the administered product should be clearly recorded in the patient file. Remove and save the pre-filled syringe label.

Turn the plunger to move the label into a position where you can remove the syringe label.

Disposal instructions



Dispose of the used syringe in a sharps container (closable, puncture resistant container).

Do not throw away any medicines via wastewater or household waste. Ask your doctor or pharmacist how to throw away medicines you no longer use. These measures will help protect the environment. Any unused product or waste material should be disposed of in accordance with local requirements.