PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

Polivy® 30 mg powder for concentrate for solution for infusion

Polivy® 140 mg powder for concentrate for solution for infusion

The active substance is polatuzumab vedotin

Contains sugar (sucrose) - Polivy 30 mg – 77 mg & Polivy 140 mg – 309 mg

Read all of this leaflet carefully before you are given Polatuzumab

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- Polivy 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.

What is in this leaflet

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

1. What Polivy is and what it is used for

What Polivy is

Polivy is a cancer medicine that contains the active substance polatuzumab vedotin.

It is always used together with other cancer medicines – see below “What other medicines is Polivy

given with".

What is Polivy used for

Polivy is given to treat "diffuse large B-cell lymphoma" that has never been treated before.

Polivy is also given to treat "diffuse large B-cell lymphoma" that has come back or has not got better:

- after at at least one previous therapy, and
- when you cannot receive a stem cell transplant.

"Diffuse large B-cell lymphoma" is a cancer that comes from "B lymphocytes" also called B-cells. These are a type of blood cells.

How Polivy works

Polivy contains something called a 'monoclonal antibody' and a substance that can kill cancer called 'MMAE'.

- The "monoclonal antibody" part of the medicine attaches to a target on B cells.
- Once attached to B cells, the medicine releases "MMAE" into the B cells and kills them.

What other medicines Polivy is given with

Polivy is given in combination with other cancer medicines:

- rituximab, cyclophosphamide, doxorubicin and prednisone for "diffuse large B-cell lymphoma" that has never been treated before.
- rituximab and bendamustine for "diffuse large B-cell lymphoma" that has come back or has not got better, after at least one previous therapy – and when you cannot receive a stem cell transplant.

2. What you need to know before you are given Polivy

You must not be given Polivy

- If you are hypersensitive (allergic) to polatuzumab vedotin or any of other ingredients of Polivy (listed in Section 6).
- if you currently have an active severe infection.

If the above applies to you, you must not be given Polivy. If you are not sure, talk to your medical practitioner or pharmacist before you are given Polivy.

Warnings and precautions

Tell your doctor, health care provider before being given the injection.

Special care should be taken with Polivy:

- you have ever had brain or nerve problems such as:
    - memory problems
    - difficulty moving or sensations in your body such as feeling pins and needles, burning, pain and discomfort even from slight touch
    - eyesight problems
- you have ever had liver problems
- you think you have an infection or have had long-lasting or repeated infections such as herpes (see “Infections” in Section 4)
- you are due to have a vaccine or you know you may need to have one in the near future.

If any of the above apply to you (or you are not sure) talk to your doctor or nurse before you are given Polivy.

Pay attention to the following side effects

Polivy can cause some serious side effects that you need to tell your doctor or nurse about straight away. These include:

Myelosuppression

Myelosuppression is a condition in which the production of blood cells is decreased, resulting in fewer red blood cells, white blood cells, and platelets. Your doctor will do blood tests to check your blood cell count.

Tell your doctor or nurse straight away if you:

- develop chills or shivering
- have a fever
- have headaches
- feel tired
- feel dizzy
- look pale
- have unusual bleeding, bruising under the skin, bleeding longer than usual after your blood has been drawn, or bleeding from your gums.

Peripheral neuropathy

Tell your doctor or nurse straight away if you have any problems with a change in the sensitivity of your skin, especially in your hands or feet, such as:

- numbness
- tingling
- a burning sensation
- pain
- discomfort or weakness
- difficulty walking.

If you had any of these symptoms before treatment with Polivy, tell your doctor straight away if you notice any changes in them.

If you have symptoms of peripheral neuropathy, your doctor may lower your dose.

Infections

Signs and symptoms of infections vary between individuals, tell your doctor or nurse straight away if you develop symptoms of an infection such as:

- fever
- cough
- chest pain
- tiredness
- painful rash
- sore throat
- burning pain when passing urine
- feeling weak or generally unwell.

Human Immunodeficiency Virus (HIV)

Polivy has not been evaluated in patients with HIV. With regard to co-administration of CYP3A-inhibitors see section 4.5.

Immunization

Live or live-attenuated vaccines should not be given concurrently with the treatment. Studies have not been conducted in patients who recently received live vaccines.

Progressive multifocal leukoencephalopathy (PML)

PML is a very rare and life threatening infection in the brain, that has occured in one patient treated with Polivy together with bendamustine and another medicine called obinutuzumab.

Tell your doctor or nurse straight away if you have:

- memory loss
- trouble speaking

- difficulty walking
- problems with your eyesight.

If you had any of these symptoms before treatment with Polivy, tell your doctor straight away if you notice any changes in them. You may need medical treatment.

Tumour lysis syndrome

Some people may develop unusual levels of some substances (such as potassium and uric acid) in the blood caused by the fast breakdown of cancer cells during treatment. This is called “tumour lysis syndrome”. Your doctor, pharmacist or nurse will do blood tests to check for the condition.

Infusion-related reactions

Infusion-related reactions, allergic or anaphylactic (more severe allergic) reactions can happen. Your doctor or nurse will check for side effects during your infusion and for 30 to 90 minutes afterwards. If you get any serious reaction, your doctor may stop treatment with Polivy.

Liver damage

This medicine can cause inflammation or damage to cells in the liver that affect the normal function of the liver. Injured liver cells may leak high amounts of certain substances (liver enzymes and bilirubin) into the bloodstream, ~~in~~ which can be detected by blood tests.

In most cases you will not have any symptoms but tell your doctor or nurse straight away if you get:

- yellowing of your skin and of the whites of your eyes (jaundice).

Your doctor will check your blood to test your liver function before and regularly during treatment.

Children and adolescents

This medicine should not be used in children or young people under the age of 18. This is because there is no information about its use in this age group.

Other medicines and Polivy

Other medicines and vaccines

Tell your doctor or nurse if you are taking, have recently taken or might start taking any other medicines. This includes medicines obtained without a prescription and herbal medicines.
Also tell your doctor or nurse if you are due to have a vaccine or you know you may need to have one in the near future.

Contraception (women and men)

If you are a woman of childbearing age, you must use effective contraception during treatment and for 9 months after the last dose of Polivy.
Men must use contraception during treatment and for 6 months after the last dose of Polivy.

Pregnancy

It is important to tell your doctor before and during treatment if you are pregnant, think you may be pregnant, or are planning to get pregnant. This is because Polivy can affect your baby's health.

Do not use this medicine if you are pregnant unless you and your doctor decide that the benefit to you outweighs possible risk to the unborn baby.

Breastfeeding

Do not breast-feed while receiving Polivy and for at least 3 months after the last dose, because small amount of Polivy may pass into your breast milk.

Fertility

Men are advised to have sperm samples preserved and stored before treatment with this medicine.

Driving and using machines

Polivy has a minor influence on your ability to drive, cycle or use any tools or machines.

- If you get infusion-related reactions or nerve damage, or if you feel tired, weak or dizzy (see section 4) do not drive, cycle or use tools or machines until the reaction stops.

See Section 4 for more information about side effects.

Important information about some of the ingredients of Polivy:

Polivy contains sugar

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking Polivy.

Polivy contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How Polivy is given

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

Polivy is given under the supervision of a doctor experienced in giving such treatments.

It is given into a vein, as a drip over 90 minutes.

How much Polivy is given

The dose of this medicine depends on your body weight.

- The usual starting dose is 1,8 mg for each kilogram of your body weight.
- If you have peripheral neuropathy, your doctor may lower your dose.

How often is Polivy given?

- Each cycle lasts 21 days
- You will be given 6 treatment cycles of Polivy in combination with other medicines.

What other medicines is Polivy given with?

- rituximab, cyclophosphamide, doxorubicin and prednisone for “diffuse large B-cell lymphoma” that has never been treated before or,
- rituximab and bendamustine for “diffuse large B-cell lymphoma” that has come back or has not got better, after at least one previous therapy – and when you cannot receive a stem cell transplant.

If you miss a dose of Polivy

- If you miss an appointment, make another one straight away.
- For the treatment to be fully effective, it is very important not to miss a dose.

If you stop receiving Polivy

Do not stop treatment with Polivy unless you have discussed this with your doctor. This is because stopping treatment may make your condition worse.

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

4. Possible side effects

Polivy can have side effects.

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

Serious side effects

Tell your doctor or nurse straight away if you notice any of the following serious side effects – you may need urgent medical treatment. These may be new symptoms or a change in your current symptoms.

- Infusion-related reactions – your doctor will check for these for 30-90 minutes afterwards
- fevers and chills
- rash/hives
- severe infections
- pneumonia (lung infection)
- herpes infection
- viral infections
- upper respiratory tract infection
- skin infection
- urinary tract infection
- unusual bleeding or bruising under the skin
- memory loss, trouble speaking, difficulty walking or problems with your eyesight
- yellowing of skin or whites of your eyes
- breathlessness and difficulty in breathing

Other side effects

Tell your doctor or nurse if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people

- pneumonia (lung infection)
- runny nose, sneezing, sore throat and cough (upper respiratory tract infection)
- numbness, tingling, a burning sensation, pain, discomfort or weakness and/or difficulty walking (peripheral neuropathy)
- fever
- cough

- vomiting
- diarrhoea or constipation
- soreness or inflammation of the mouth and/or gut (mucositis)
- feeling sick (nausea)
- abdominal (belly) pain
- feeling tired
- not feeling hungry
- loss of weight
- infusion-related reactions
- common cold
- hair loss
- changes in blood tests:
  - low levels of all types of white blood cell (combined)
  - low levels of neutrophils (a type of white blood cell) with or without fever
  - low level of platelets (a type of blood cell that helps your blood to clot)
  - low levels of red blood cells (anaemia)
  - low level of potassium in the blood (hypokalaemia)

Common: may affect up to 1 in 10 people

- severe infection (sepsis)
- urinary tract infection
- viral infections
- herpes infection
- skin infection
- inflammation of the lungs
- breathlessness and difficulty in breathing
- dizziness
- fluid retention causing swelling in the lower legs or hands (oedema peripheral)

- high level of transaminases in the blood
- joint pain
- itchiness
- chills
- rash
- dry skin
- muscle pain
- changes shown in blood tests:
  - decreased number of all blood cells (pancytopenia)
  - low levels of lymphocytes (a type of white blood cells)
  - low level of phosphate in the blood (hypophosphataemia)
  - low level of calcium in the blood (hypocalcaemia)
  - low level of albumin in the blood (hypoalbuminemia)
  - high level of lipase enzyme in the blood

Uncommon: may affect up to 1 in 100 people

- blurred vision

Tell your doctor or nurse straight away if you notice any side effects listed above.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the “6.04 Adverse Medicine Reaction Report 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 Polivy.

5. How to store Polivy

Polivy will be stored by the healthcare professionals at the hospital or clinic. The storage details are as follows

- Store all medicines out of reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and the vial after EXP. The expiry date refers to the last day of that month.
- Store at or between 2 °C – 8 °C (in a refrigerator)
- Do not freeze.
- Keep the container in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or 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 Polivy contains

- The active substance is polatuzumab vedotin.
- Polivy 30 mg: Each vial contains 30 milligrams (mg) polatuzumab vedotin.
- Polivy 140 mg: Each vial contains 140 milligrams (mg) polatuzumab vedotin.
- After reconstitution each millilitre (mL) contains 20 mg polatuzumab vedotin.
- The other ingredients are: polysorbate 20, sodium hydroxide, succinic acid, sucrose.

What Polivy looks like and contents of the pack

Polivy powder for concentrate for solution for infusion is a white to slightly grayish-white cake provided in a glass vial.

Each pack of Polivy consists of one vial.

Holder of Certificate of Registration

Roche Products (Pty) Ltd

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Roche Ethical Assistance Line (REAL) toll-free: 0800 21 21 25

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Polivy 30 mg : 56/26/0149

Polivy 140 mg : 56/26/0150

Instructions for Use

The following information is intended for healthcare professionals only:

Procedures for proper handling and disposal of anticancer medicinal products should be considered.

Instructions for reconstitution

- **Polivy 30 mg:** Using a sterile syringe, slowly inject 1.8 mL of sterile water for injection into the 30 mg Polivy vial to yield a single-dose solution containing 20 mg/mL polatuzumab vedotin. Direct the stream toward the wall of the vial and not directly on the lyophilized cake.
- **Polivy 140 mg:** Using a sterile syringe, slowly inject 7,2 mL of sterile water for injection into the 140 mg Polivy vial to yield a single-dose solution containing 20 mg/mL polatuzumab vedotin. Direct the stream toward the wall of the vial and not directly on the lyophilized cake.
- Swirl the vial gently until completely dissolved. Do not shake.
- Inspect the reconstituted solution for discoloration and particulate matter. The reconstituted solution should appear colourless to slightly brown, clear to slightly opalescent, and free of visible particulates. Do not use if the reconstituted solution is discoloured, is cloudy, or contains visible particulates.

Instructions for dilution

1. Polivy must be diluted to a final concentration of 0,72 – 2,7 mg/mL in an intravenous infusion bag, with a minimum volume of 50 mL, containing 9 mg/mL sodium chloride solution for injection, or 4,5 mg/mL sodium chloride solution for injection, or 5 % glucose.
2. Determine the volume of 20 mg/mL reconstituted solution needed based on the required dose (see below):

Total Polivy dose (mL) to be further diluted =	Polivy dose (mg/kg) X patient's weight (kg) / Reconstituted vial concentration (20 mg/mL)

3. Withdraw the required volume of reconstituted solution from the Polivy vial using a sterile syringe and dilute into the intravenous infusion bag. Discard any unused portion left in the vial.
4. Gently mix the intravenous bag by slowly inverting the bag. Do not shake.
5. Inspect the intravenous bag for particulates and discard if present.

Reconstituted solution

From a microbiological point of view, the reconstituted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours refrigerated (2 °C - 8 °C), unless reconstitution has taken place in controlled and validated aseptic conditions. Chemical and physical in-use stability of the reconstituted solution has been demonstrated for up to 72 hours refrigerated (2 °C - 8 °C) and up to 24 hours at room temperature (9 °C - 25 °C).

Diluted solution

From a microbiological point of view, the prepared solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours refrigerated (2 °C - 8 °C), unless dilution has taken place in controlled and validated aseptic conditions. Chemical and physical stability of the prepared solution for infusion has been demonstrated for the durations listed in Table 1. Discard diluted Polivy solution if storage time exceeds the limits specified in Table 1.

Table 1 Durations for which chemical and physical stability of the prepared solution for infusion have been demonstrated

Diluent used to prepare solution for infusion	**Solution for infusion storage conditions[1]**
Sodium chloride 9 mg/mL (0,9 %)	Up to 72 hours refrigerated (2 °C - 8 °C) or up to 4 hours at room temperature (9 °C - 25 °C)
Sodium chloride 4,5 mg/mL (0,45 %)	Up to 72 hours refrigerated (2 °C - 8 °C) or up to 8 hours at room temperature (9 °C - 25 °C)
5 % Glucose	Up to 72 hours refrigerated (2 °C - 8 °C) or up to 8 hours at room temperature (9 °C - 25 °C)

[1] To ensure product stability, do not exceed specified storage durations.