
PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

YERVOY® 5 mg/ml solution for infusion

Ipilimumab

Contains sugar (mannitol): 107 mg per 10 ml vial and 426 mg per 40 ml vial

Read all of this leaflet carefully before you are given YERVOY

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- **YERVOY** 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 YERVOY is and what it is used for
2. What you need to know before you use YERVOY
3. How to use YERVOY
4. Possible side effects
5. How to store YERVOY
6. Contents of the pack and other information

1. What YERVOY is and what it is used for

YERVOY contains the active substance ipilimumab, a protein which helps your immune system to attack and destroy cancer cells by your immune cells.

YERVOY is used to treat advanced melanoma (a type of skin cancer) in adults.

2. What you need to know before you use YERVOY

YERVOY should not be administered to you:

- if you are hypersensitive (allergic) to ipilimumab or any of the other ingredients of **YERVOY** (listed in section 6).

Warnings and precautions

Tell your doctor or healthcare provider before being given the injection:

YERVOY may cause:

- **problems with your heart** such as a change in the rhythm or rate of the heartbeat or an abnormal heart rhythm.
- **inflammation of the intestines (colitis)** which can worsen to bleedings or bowel perforation. Signs and symptoms of colitis may include diarrhoea (watery, loose or soft stools), an increased number of bowel movements than usual, blood in your stools or darker-coloured stools, pain or tenderness in your stomach area.
- **problems with your lungs** such as breathing difficulties or cough. These may be signs of inflammation of the lungs (pneumonitis or interstitial lung disease).
- **inflammation of the liver (hepatitis)** that can lead to liver failure. Signs and symptoms of hepatitis may include eye or skin yellowing (jaundice), pain on the right side of your stomach area, tiredness.
- **inflammation of the skin** that can lead to severe skin reaction (known as toxic epidermal necrolysis, Stevens-Johnson syndrome and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)). Signs and symptoms of severe skin reaction may include skin rash with or without itching, peeling of the skin, dry skin, fever, fatigue, swelling of the face or lymph glands, increase of eosinophils (type of white blood cells) and effects on liver, kidneys or lungs. Please note that the reaction called DRESS may develop weeks or

months after your last dose.

- **inflammation of the nerves** that can lead to paralysis. Symptoms of nerve problems may include muscle weakness, numbness or tingling in your hands or feet, loss of consciousness or difficulty waking up.
- **inflammation or problems with your kidneys.** Signs and symptoms may include abnormal kidney function tests, or decreased volume of urine.
- **inflammation of hormone producing glands** (especially the pituitary, adrenal and thyroid glands) that may affect how these glands work. Signs and symptoms that your glands are not working properly may include headaches, blurry or double vision, tiredness, decreased sexual drive, behavioural changes, dizziness or lightheadedness, sweating, rapid heart rate, weight loss or weight gain.
- **Type 1 Diabetes, including diabetic ketoacidosis** (acid in the blood produced from diabetes)
- **inflammation of the muscles** such as myocarditis (inflammation of the heart muscle) and myositis (inflammation of the muscles). Signs and symptoms may include muscle pain, stiffness, weakness, chest pain, or severe fatigue.
- **inflammation of the eyes.** Signs and symptoms may include redness in the eye, pain in the eye, vision problems, blurry vision or temporary loss of sight.
- **haemophagocytic lymphohistiocytosis (HLH).** A rare disease in which our immune system makes too many of otherwise normal infection fighting cells called histiocytes and lymphocytes. Symptoms may include enlarged liver and/or spleen, skin rash, lymph node enlargement, breathing problems, easy bruising, kidney abnormalities, and heart problems.

Tell your doctor immediately if you have any of these signs or symptoms or they get worse. **Do not try to treat your symptoms with other medicines.** Your doctor may give you other medicines in order to prevent more severe complications and reduce your symptoms, withhold the next dose of **YERVOY**, or stop your treatment with **YERVOY** altogether.

Please note that these signs and symptoms are **sometimes delayed** and may develop weeks or months after your last dose. Before treatment, your doctor will check your general health. You will also have **blood tests** during treatment.

Check with your doctor or healthcare professional before you are given YERVOY:

- if you have an **autoimmune disease** (a condition where the body attacks its own cells)
- if you have, or have ever had, **chronic viral infection of the liver**, including hepatitis B (HBV) or hepatitis C (HCV)
- if you have **human immunodeficiency virus (HIV)** infection or acquired immune deficiency syndrome (AIDS)
- if you have previously experienced a severe skin adverse reaction on a prior cancer therapy
- if you have any history of inflammation of the lungs
- if you have, or have ever had, tuberculosis
- if you were treated for bladder cancer with immunotherapy called BCG

Children and adolescents

YERVOY should not be used in children below 18 years of age.

Other medicines and YERVOY

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

Before you are given YERVOY, tell your doctor:

- if you are taking any medicines that suppress your immune system, such as corticosteroids. These medicines may interfere with the effect of **YERVOY**. However, once you are treated with **YERVOY**, your doctor may give you corticosteroids to reduce the side effects that you may have with **YERVOY**.
- if you are taking any medicines that stop your blood from clotting (anticoagulants). These medicines may increase the likelihood of bleeding in the stomach or intestine, which is a side effect of **YERVOY**.
- if you have recently been prescribed vemurafenib, another medicine for the treatment of skin cancer). When **YERVOY** is given following prior vemurafenib there may be an increased risk of skin side-effects.

Do not take any other medicines during your treatment without talking to your doctor first. Based on early data, the combination of **YERVOY** and vemurafenib is not recommended due to increased toxicity to the liver.

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 healthcare provider for advice before receiving **YERVOY**.

Do not use **YERVOY** if you are pregnant. The active substance, ipilimumab, could harm an unborn baby.

- You must use highly effective contraception while you are being treated with **YERVOY** if you are a woman who could become pregnant.
- If you become pregnant while using **YERVOY** tell your doctor.

You should not breastfeed your baby when receiving **YERVOY**.

Driving and using machines

Do not drive, cycle or use machines after you have been given **YERVOY** unless you are sure you are feeling well. Feeling tired or weak is a very common side effect of **YERVOY**. This can affect your ability to drive, cycle or to use machines.

YERVOY contains sodium

Tell your doctor if you are on a low-sodium (low-salt) diet before you are given **YERVOY**. It contains 2,3 mg sodium per ml of concentrate.

3. How to use YERVOY

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

How YERVOY is given

You will not be expected to give yourself **YERVOY**. It will be given to you by a person who is qualified to do so. **YERVOY** will be given to you in a hospital or clinic under the supervision of an experienced doctor. It will be given to you as an infusion (a drip) into a vein (intravenously) over a period of 90 minutes.

How much YERVOY is given

The recommended dose is 3 mg of ipilimumab per kilogram of your body weight. The amount of **YERVOY** you will be given will be calculated based on your body weight. Depending on your dose, some or all of the content of the **YERVOY** vial may be diluted with sodium chloride 9 mg/ml (0,9 %) solution for injection or 50 mg/ml (5 %) glucose solution for injection before use. More than one vial may be necessary to obtain the required dose.

You will be treated with **YERVOY** once every 3 weeks, for a total of 4 doses.

You may notice the appearance of new lesions or growth of existing lesions on your skin, which can be expected when you are being treated with **YERVOY**.

Your doctor will continue giving you **YERVOY** for a total of 4 doses, depending on your tolerance to the treatment.

If you receive more YERVOY than you should

Since a healthcare professional will administer **YERVOY**, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you miss a dose of YERVOY

It is very important for you to keep all your appointments to receive **YERVOY**. If you miss an appointment, ask your doctor when to schedule your next dose.

If you stop using YERVOY

Stopping your treatment may stop the effect of **YERVOY**. Do not stop treatment with **YERVOY** unless you have discussed this with your doctor.

If you have any further questions about your treatment or the use of **YERVOY**, ask your doctor.

4. Possible side effects

YERVOY can have side effects.

Not all side effects reported for YERVOY are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while receiving YERVOY, please consult your doctor, pharmacist or other healthcare professional for advice.

Be aware of important symptoms of inflammation.

YERVOY acts on your immune system and may cause **inflammation** in parts of your body. Inflammation may cause serious damage to your body and some inflammatory conditions may be life-threatening. **YERVOY** can also cause hypersensitivity (allergic) reactions.

Tell your doctor immediately if you get any of the following side effects.

Do not try to treat your symptoms with other medicines.

The following side effects have been reported in patients receiving **YERVOY**:

Very common side effects

- loss of appetite
- diarrhoea (watery, loose or soft stools), vomiting or feeling sick (nausea), constipation, stomach pain
- skin rash, itching
- pain in the muscles, bones, ligaments, tendons, and nerves
- feeling tired or weak, reaction at site of injection, fever, oedema (swelling), pain

Common side effects

- serious bacterial infection of the blood (sepsis), infection of the urinary tract, infection of the respiratory tract
- tumour pain
- A decreased number of red blood cells (which carry oxygen), white blood cells (which are important in fighting infection) or platelets (cells which help the blood to clot).
- underactive function of the thyroid gland which can cause tiredness or weight gain, underactive function (hypopituitarism) or inflammation (hypophysitis) of the pituitary gland situated at the base of the brain
- dehydration
- confusion, depression
- excessive accumulation of fluid in the brain, damage to the nerves (causing pain, weakness and cramps), dizziness, headache
- blurred vision, pain in the eye
- irregular or abnormal heartbeat

- low blood pressure, temporary redness of the face and neck, feeling of intense heat with sweating and rapid heartbeat
- shortness of breath (dyspnoea), cough, hay fever
- bleeding in the stomach or intestine, inflammation of the intestines (colitis), heartburn, mouth ulcers and cold sores (stomatitis)
- abnormal function of the liver
- inflammation of the inner surface lining of a particular organ
- inflammation and redness of the skin, skin colour change in patches (vitiligo), hives (itchy, bumpy rash), hair loss or thinning, excessive sweating at night, dry skin
- pain in muscles and joints (arthralgia), muscle spasms, inflammation of the joints (arthritis)
- kidney function failure
- shivering, lack of energy
- flu-like illness
- decrease in body weight

Uncommon side effects:

- serious bacterial infection of the blood (septic shock), inflammation around the brain or spinal cord, inflammation of the stomach and intestines, inflammation of bowel wall (causing fever, vomiting and stomach pain), lung infection
- a group of symptoms due to cancer in the body such as high blood levels of calcium and cholesterol, and low blood levels of sugar (paraneoplastic syndrome)
- increase of eosinophils (type of white blood cells)
- allergic reaction

- decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys), overactive function of the thyroid gland, which can cause rapid heart rate, sweating and weight loss, defect of the glands producing sex hormones
- decreased function of the adrenal glands caused by an underactive hypothalamus (part of the brain)
- a group of metabolic complications occurring after cancer treatment characterised by high blood levels of potassium and phosphate, and low blood levels of calcium (tumour lysis syndrome)
- changes in mental health, lowered sex drive
- severe and possibly fatal inflammation of the nerves causing pain, weakness or paralysis in the extremities (Guillain-Barré syndrome), fainting, inflammation of the nerves within the brain, difficulty in coordinating movements (ataxia), shaking, brief involuntary muscle contraction, difficulty in speaking
- inflammation of the eye (conjunctivitis), bleeding in the eye, inflammation of the coloured part of the eye, reduced vision, a foreign body sensation in the eyes, swollen runny eyes, swelling of the eye, inflammation of the eye lids
- inflammation of the blood vessels, disease of the blood vessels, restriction in the blood supply to the extremities, low blood pressure when standing up
- extreme difficulty in breathing, fluid accumulation in the lungs, inflammation of the lungs
- bowel perforation, inflammation of the small intestine, inflammation of the bowel or the pancreas (pancreatitis), peptic ulcer, inflammation of the food pipe, blockage of the intestines, inflammation of the anus and the rectal wall (marked by bloody stools and a frequent urge to defecate)
- liver failure, inflammation of the liver, enlarged liver, yellowing of the skin or eyes (jaundice)
- severe and possibly fatal peeling of the skin (toxic epidermal necrolysis)
- inflammation of the muscles causing pain or stiffness in the hip and shoulder
- inflammation of the kidney, or the central nervous system
- multi organ inflammation

- inflammation of skeletal muscles
- muscle weakness
- kidney disease
- absence of menstrual periods
- multi organ dysfunction, reaction related to infusion of the medicine
- change in hair colour
- inflammation of the bladder, signs and symptoms may include frequent and/or painful urination, urge to pass urine, blood in urine, pain and pressure in lower abdomen

Rare side effects

- inflammatory disease of blood vessels (most commonly head arteries)
- swelling of the thyroid gland (thyroiditis)
- skin disease characterized by dry red patches covered with scales (psoriasis)
- inflammation and redness of the skin (erythema multiforme)
- a type of severe skin reaction characterized by rash accompanied by one or more of the following features: fever, swelling of the face or lymph glands, increase of eosinophils (type of white blood cells), effects on liver, kidneys or lungs (a reaction called DRESS).
- an inflammatory disorder (most likely of autoimmune origin) affecting the eyes, skin and the membranes of the ears, brain and spinal cord (Vogt-Koyanagi-Harada syndrome), loosening of membrane at the back of the eye (serous retinal detachment)
- symptoms of type 1 diabetes or diabetic ketoacidosis include feeling more hungry or thirsty than usual, needing to urinate more often, weight loss, feeling tired, feeling sick, stomach pain, fast and deep breathing, confusion, unusual sleepiness, a sweet smell to your breath, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat

- muscle weakness and tiredness without atrophy (myasthenia gravis)
- serious, potential life-threatening allergic reaction
- coeliac disease (characterized by symptoms such as stomach pain, diarrhoea, and bloating after consuming gluten-containing foods)

In addition, the following uncommon side effects have been reported in patients who received doses other than 3 mg/kg of **YERVOY** in clinical trials.

- triad of symptoms (meningism): neck stiffness, intolerance of bright light and headache, flu-like discomfort
- inflammation of the heart muscle, weakness of the heart muscle, fluid around the heart
- inflammation of the liver or the pancreas, nodules of inflammatory cells in various organs of your body
- infection within the abdomen
- painful skin lesions of the arms and legs and face (erythema nodosum)
- overactive pituitary gland
- decreased function of the parathyroid gland
- inflammation of the eye, eye muscle inflammation
- decreased hearing
- poor blood circulation which makes toes and fingers numb or pale
- damage to the tissues of the hands and feet resulting in redness, swelling and blisters

Other side effects that have been reported (frequency not known) include:

- Organ transplant rejection
- a type of skin blistering disease (called pemphigoid)
- a condition where the immune system makes too many infection-fighting cells called histiocytes and lymphocytes that may cause various symptoms (called haemophagocytic lymphohistiocytosis). Symptoms

may include enlarged liver and/or spleen, skin rash, lymph node enlargement, breathing problems, easy bruising, kidney abnormalities, and heart problems.

- pain, numbness, tingling, or weakness in the arms or legs; bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating and constipation (myelitis)

Changes in test results

YERVOY may cause changes in the results of tests carried out by your doctor. These include:

- a variation in the number of red blood cells (which carry oxygen), white blood cells (which are important in fighting infection) or platelets (cells which help the blood to clot)
- an abnormal variation of hormones and liver enzyme levels in the blood
- abnormal liver function test
- abnormal levels of calcium, sodium, phosphate or potassium in the blood
- presence of blood or proteins in the urine
- an abnormally high alkalinity of the blood and other body tissues
- kidneys unable to remove acids from blood normally
- presence of antibodies in the blood against some of your own cells

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, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

By reporting side effects, you can help provide more information on the safety of **YERVOY**.

5. How to store YERVOY

Store all medicines out of reach of children.

Store in a refrigerator (2 °C – 8 °C).

Store in the original package in order to protect from light.

Do not freeze.

For single use only. Discard any unused portion.

Once opened, the product should be infused or diluted and infused immediately. The chemical and physical in-use stability of the undiluted or diluted concentrate (between 1 mg/ml and 4 mg/ml) has been demonstrated for 24 hours at 25 °C and 2 °C to 8 °C. If not used immediately, the infusion solution (undiluted or diluted) may be stored for up to 24 hours either under refrigeration (2 °C to 8 °C) or at room temperature (25 °C).

Do not use **YERVOY** after the expiry date which is stated on the carton and the vial label after EXP. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What YERVOY contains

The active substance is ipilimumab.

Each ml of concentrate contains 5 mg ipilimumab.

One 10 ml vial contains 50 mg of ipilimumab.

One 40 ml vial contains 200 mg of ipilimumab.

The other ingredients are Tris-hydrochloride, sodium chloride (see section 2 "**YERVOY** contains sodium"), mannitol (E421), pentetic acid, polysorbate 80, sodium hydroxide, hydrochloric acid and water for injections.

What YERVOY looks like and contents of the pack

YERVOY is a sterile, preservative-free, clear to slightly opalescent, colourless to pale yellow solution for intravenous infusion, which may contain a small amount of visible translucent to white particulates.

YERVOY is available in:

10 ml of 5 mg/ml sterile concentrate in a clear, colourless vial (Type I glass) with a grey stopper (coated butyl rubber) and a light blue flip-off seal (aluminium). Pack size of 1.

OR

40 ml of 5 mg/ml sterile concentrate in a clear, colourless vial (Type I glass) with a grey stopper (coated butyl rubber) and a purple flip-off seal (aluminium). Pack size of 1.

Holder of Certificate of Registration

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Access to the corresponding Professional Information

An electronic copy of the Professional Information (PI) is available on the Equity website

<http://www.equitypharmaceuticals.co.za> or <http://www.sahpra.org.za>.

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