

YERVOY®

(yure-voy)

Ipilimumab (ipi-lim-u-mab)

Consumer Medicine Information

WARNINGS AND PRECAUTIONS

Both YERVOY and OPDIVO act 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.

These side effects are most likely to begin during treatment, however, side effects can show up months after your last infusion.

IT IS IMPORTANT TO TELL YOUR DOCTOR IF YOU HAVE, OR DEVELOP, ANY OF THE SYMPTOMS LISTED UNDER POSSIBLE SIDE EFFECTS.

WHAT IS IN THIS LEAFLET

This leaflet answers some common questions about YERVOY. It does not contain all of the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you receiving YERVOY against the benefits they expect it will have for you.

If you have any concerns about taking this medicine, ask your doctor.

You should read this leaflet carefully and keep it in a safe place to refer to it later.

WHAT IS YERVOY USED FOR

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

Treatment with YERVOY

YERVOY, as a single therapy, is used to treat advanced skin cancer (unresectable or metastatic melanoma) in adults.

Treatment with YERVOY in combination with OPDIVO

YERVOY in combination with OPDIVO (nivolumab) is used to treat advanced skin cancer (unresectable or metastatic melanoma) and a type of advanced kidney cancer (renal cell carcinoma).

This medicine is available only with a doctor's prescription.

YERVOY will be given to you in hospital under the supervision of an experienced doctor.

Ask your doctor if you have any questions about why YERVOY has been prescribed for you.

BEFORE YOU ARE GIVEN YERVOY

You should not be given YERVOY

- if you are allergic (hypersensitive) to ipilimumab or any of the other ingredients of YERVOY. If you are not sure, talk to your doctor.

Check with your doctor or nurse before you are given YERVOY

- if you take corticosteroids or immunosuppressive therapy. These are medicines which reduce the functioning of your immune system, and may make you more likely to develop infections and some cancers
- 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 a human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS)
- if you take anticoagulant therapy. These are medicines which increase the risk of bleeding in the stomach and gut

- if you have previously experienced a severe skin reaction on prior cancer therapy
- if you have any history of inflammation of the lungs.

YERVOY may cause:

- Problems with your heart such as changes in rhythm or rate of the heart beat or an abnormal heart rhythm.
- Bowel, intestine and stomach inflammation which can worsen to bleeding or bowel perforation. Signs and symptoms may include diarrhoea (watery, loose or soft stools), an increased number of bowel movements (an increase by two or more per day), constipation, 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).
- Liver damage or hepatitis. Signs and symptoms may include yellowing of your skin or the whites of your eyes (jaundice), pain in your stomach area, excessive sleepiness
- Skin rash or itching. 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. Severe skin reactions can include toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS) and

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

- Inflammation of the nerves. Symptoms may include muscle weakness or decreased strength, numbness or tingling in your hands or feet, loss of consciousness or difficulty waking up.
- Inflammation or problems with your kidney. Signs and symptoms may include abnormal kidney function tests, or decreased volume of urine
- Damage or inflammation of hormone producing glands. Symptoms may include headaches, blurry or double vision, fatigue, decreased sexual drive, behavioural changes
- Diabetes. Symptoms include excessive thirst, the passing of a greatly increased amount of urine, increase in appetite with a loss of weight, feeling tired, drowsy, weak, depressed, irritable and generally unwell) or diabetic ketoacidosis (acid in the blood produced from diabetes).
- Inflammation of the muscles. Signs and symptoms may include muscle pain, stiffness, weakness, chest pain or severe fatigue. This may include myocarditis (inflammation of the heart muscle), myositis (inflammation of the muscles) and rhabdomyolysis (stiffness in muscle and joints, muscle spasm).
- Eye inflammation. Symptoms may include redness in the eye, pain in the eye, vision changes or blurry vision.

- Solid organ transplant rejection.

Complications of stem cell transplant that uses donor cells (allogeneic) may occur. These complications can be severe and can lead to death. Your healthcare provider will monitor you for signs of complications if you have an allogeneic stem cell transplant.

Using other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Ask your doctor for advice before taking any medicine during your treatment.

Children

It is not recommended to use this medicine in children or adolescents (below 18 years) until further information becomes available.

Take special care with YERVOY

YERVOY is a medicine that influences your immune system and may cause inflammation in parts of your body.

Inflammation can cause serious damage to your body and some inflammatory conditions may be irreversible or life-threatening. Some inflammatory conditions may need treatment or withdrawal of YERVOY. Tell your doctor immediately if you have any of the symptoms of inflammation listed in "Possible Side Effects" in this leaflet.

Pregnancy and breast-feeding

Tell your doctor if you are pregnant, planning to become pregnant, or if you are breast-feeding.

You must not use YERVOY if you are pregnant unless your doctor specifically recommends it.

The effects of YERVOY in pregnant women are not known, but it is possible that the active substance, ipilimumab, could harm an unborn baby.

- You must use 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 stop breast-feeding if you are being treated with YERVOY.

It is not known whether ipilimumab gets into breast milk. A risk to the breast-fed infant cannot be excluded.

Driving and using machines

Do not drive or use machines after you have been given YERVOY unless you are sure that you are not affected.

Feeling tired or weak is a very common side effect of YERVOY. This can affect your ability to drive or operate any machinery. Patients should therefore be cautious after having received YERVOY.

Important information about some of the ingredients of YERVOY

Tell your doctor if you are on a low-sodium (low-salt) diet before you are given YERVOY. This medicine contains 2.3 mg sodium per mL of concentrate.

HOW YERVOY IS GIVEN

YERVOY will be given to you in 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).

Your doctor will decide how many treatments you need.

Dosage and frequency of administration

The recommended dose and frequency of YERVOY can be different depending on the type of cancer it is being used to treat.

Some types of cancer are treated with YERVOY in combination with OPDIVO.

Your doctor will advise you if you will be given both treatments and will tell you about the dose and frequency of these treatments.

Please refer to the Consumer Medicines Information leaflet of OPDIVO in order to understand its use. If you have questions about this medicine, please ask your doctor.

If you miss a dose of YERVOY

It is very important for you to keep all 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 the medicine. 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 this medicine, ask your doctor.

WHILE YOU ARE BEING TREATED WITH YERVOY

Things you must do

Tell your doctor immediately if you have any signs or symptoms of possible side effects or if they get worse.

Do not try to treat your symptoms with other medicines on your own.

You doctor may:

- Give you other medicines in order to prevent 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.

Tell any other doctors, dentists, and pharmacists who are treating you that you are being given YERVOY.

If you are about to be started on any new medicine, tell your doctor, dentist or pharmacist that you are being given YERVOY.

Tell your doctor immediately if you develop symptoms of an allergic reaction.

These symptoms may be:

- shortness of breath, wheezing or difficulty breathing
- swelling of the face, lips, tongue or other parts of the body
- rash, itching or hives on the skin

POSSIBLE SIDE EFFECTS

Like all medicines, YERVOY can cause side effects, although not everybody gets them. Your doctor will discuss these with you and will explain the risks and benefits of your treatment.

The following side effects have been reported in clinical trials when YERVOY was used alone:

Very common side effects (affects more than 1 user in 10)

- loss of appetite
- diarrhoea
- feeling sick (nausea) or being sick (vomiting)
- stomach pain
- itching, skin rash
- feeling tired or weak
- cough
- headache
- fever
- insomnia

Tell your doctor immediately if you get any of these side effects. Do not try to treat your symptoms with other medicines.

Common side effects (affects 1 to 10 users in 100)

- serious bacterial infection of the blood (sepsis)
- tumour pain
- underactive function of pituitary gland (hypopituitarism), the adrenal glands, or underactive function of the thyroid gland (hypothyroidism) which can cause tiredness or weight gain
- overactive function of the thyroid gland (hyperthyroidism), which can cause rapid heart rate, sweating and weight loss
- dehydration
- inflammation of the eye which causes pain and redness, blurred vision
- low blood pressure, temporary redness of the face and neck
- shortness of breath, bleeding in the stomach or intestine (gut), inflammation of the colon (large bowel), constipation
- weight loss
- abnormal function of the liver
- inflammation and redness of the skin, skin colour change in patches (vitiligo), hair loss or thinning,

- excessive sweating at night
- pain in muscles and joints
- kidney function failure
- fever, shivering, lack of energy,
- swelling, pain, reaction at site of injection,
- confusion
- increase in alkaline phosphatase (an enzyme released by the liver)
- influenza like illness

Uncommon side effects (affects 1 to 10 users in 1,000)

- serious bacterial infection of the blood (sepsis, septic shock)
- urinary tract infection, kidney disease, kidney function failure
- inflammation of the stomach and intestines
- depression, lowered sex drive,
- inflammation of blood vessels in the skin, hives (itchy, bumpy rash), painful skin lesions of the arms, legs and face
- muscle spasms, painful joints, muscle inflammation

- change or absence of menstrual periods
- pain in the eye, reduced vision, bleeding in the eye, a foreign body sensation in the eyes, inflammation of the eye muscle, swollen runny eyes
- irregular or abnormal heart beat
- extreme difficulty breathing, inflammation of the lungs, fluid in the lungs, hay fever
- disease of blood vessels, low blood pressure, feeling of intense heat with sweating and rapid heart beat, weakness of the heart muscle, fluid around the heart
- damage to the nerves (causing pain, weakness and cramps), dizziness, brief involuntary muscle contraction, shaking, excessive accumulation of water in the brain, disease of nerves in the head, difficulty in speaking, difficulty in coordinating movements (ataxia)
- bowel perforation, stomach wall membrane inflammation, inflammation of the duodenum, of the bowel or of the pancreas, heartburn
- a group of metabolic complications occurring after cancer treatment
- liver failure, enlarged liver, inflammation of the liver, thyroid gland, kidney, pancreas or central nervous system, nodules of inflammatory cells in various organs of your body, immune-related effects of the inner surface lining of a particular organ, yellowing of the skin or eyes (jaundice)

- reaction related to infusion, multi-organ failure
- reduction of red blood cells
- multi organ inflammation
- decreased hearing
- change in hair colour
- mucosal inflammation
- infusion related reaction

Rare side effects (affects 1 to 10 users in 10,000)

- infection of the airways or of the upper respiratory tract
- infection around the brain or spinal cord
- allergic reaction (shock)
- decreased function of the adrenal glands caused by an underactive hypothalamus (part of the brain) or an overactive pituitary gland (a small gland at the base of the brain), defect in glands producing sex hormones
- antibodies against some of your own body cells causing damage to the thyroid gland or inflammation of the kidney or brain
- changes in mental health

- inflammation of the nerves (causing pain, weakness or paralysis in the extremities), drowsiness or lack of energy
- triad of symptoms (meningism): neck stiffness, intolerance of bright light and headache
- inflammation of the eye, swollen runny eyes, inflammation of the coloured part of the eye, swelling of the eye
- inflammation of the heart muscle, disease of the heart muscle, irregular heart beat
- restriction in blood supply of the extremities, inflammatory destruction of blood vessels, inflammatory disease of blood vessels (most commonly head arteries), poor blood circulation which makes toes and fingers numb or pale
- breathing failure caused by fluid in the lungs
- inflammatory disease of the intestines (causing abdominal pain, diarrhoea which may be bloody, vomiting or weight loss)
- peeling skin
- inflammation of muscles, causing pain or stiffness in hip and shoulder
- hearing disorder
- blood disorder caused by overactive immune cells.

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

The following side effects have been reported with YERVOY in combination with OPDIVO:

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

- Overactive thyroid gland, which can cause rapid heart rate, sweating and weight loss

- Underactive thyroid gland, which can cause tiredness or weight gain
- Decreased appetite
- Headache
- Shortness of breath (dyspnoea)
- Inflammation of the intestines (colitis), diarrhoea (watery, loose or soft stools), vomiting, nausea, stomach pain
- Skin rash sometimes with blisters, itching
- Pain in the joints, muscles and bones
- Feeling tired or weak
- Fever

Common (may affect up to 1 in 10 people)

- Serious lung infection (pneumonia), infections of the upper respiratory tract
- Increase in some white blood cells
- Decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys); underactive function (hypopituitarism) or inflammation (hypophysitis) of the pituitary gland situated at the base of the brain; overactive thyroid gland, which can cause rapid heart rate, sweating and weight loss; inflammation of the thyroid gland (hyperthyroidism); swelling of the thyroid gland

- Dehydration
- Inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; dizziness
- Inflammation of the eye, which causes pain and redness, blurred vision
- Fast heart rate
- High blood pressure (hypertension)
- Inflammation of the lungs (pneumonitis), characterised by coughing and difficulty breathing, blood clots, cough
- Mouth ulcers and cold sores (stomatitis), inflammation of the pancreas (pancreatitis), constipation, dry mouth
- Inflammation of the liver
- Skin colour change in patches (vitiligo), dry skin, redness of the skin, unusual hair loss or thinning, hives (itchy rash)
- Pain in the muscles and bones
- Kidney failure (including abrupt loss of kidney function)
- Oedema (swelling), pain
- Allergic reaction, reactions related to the infusion of the medicine

Uncommon (may affect up to 1 in 100 people)

- Inflammation of the brain
- Bronchitis
- Chronic diseases associated with a build-up of inflammatory cells in various organs and tissues, most commonly the lungs (sarcoidosis)
- Acid in the blood produced from diabetes (diabetic ketoacidosis), diabetes
- A temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain-Barré syndrome); damage to nerves causing numbness and weakness (polyneuropathy); inflammation of the nerves; foot drop (peroneal nerve palsy); inflammation of the nerves caused by the body attacking itself, causing numbness, weakness, tingling or burning pain (autoimmune neuropathy)
- Changes in the rhythm or rate of the heart beat, abnormal heart rhythm
- Fluid around the lungs
- Intestinal perforation, inflammation of the stomach (gastritis), inflammation of the duodenum (duodenitis)
- Skin disease with thickened patches of red skin, often with silvery scales (psoriasis)
- Chronic disease of joints (spondyloarthropathy)

- Disease in which the immune system attacks the glands that make moisture for the body, such as tears and saliva (Sjogren's syndrome)
- Inflammation of the joints (arthritis)
- Inflammation of muscles (myositis) causing pain or stiffness
- Inflammation of the kidney (nephritis)
- Chest pain
- Inflammation of the heart (myocarditis) characterised by shortness of breath, fatigue, palpitations or chest pain.
- Muscle breakdown/injury (rhabdomyolysis) characterised by muscle pain, weakness, nausea or vomiting.

Rare (may affect up to 1 in 1000 people)

- Severe and possibly fatal peeling of the skin (toxic epidermal necrolysis, Steven-Johnson syndrome)

Changes in test results

- YERVOY in combination with OPDIVO may cause changes in the results of tests carried out by your doctor. These include:
 - Abnormal liver function tests
 - Abnormal kidney function tests

- 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)
- An increased level of the enzyme that breaks down fats and of the enzyme that breaks down starch.
- Abnormal levels of calcium, potassium, magnesium or sodium in your blood
- Higher blood levels of bilirubin
- Decrease in body weight
- Higher (hyperglycaemia) or lower (hypoglycaemia) levels of sugar in your blood

If any of the side effects listed in this leaflet appear or worsen, or if you notice any side effects not listed in this leaflet, please tell your doctor.

Do not be alarmed by possible side effects.

You may not experience any of them.

Ask your doctor to answer any questions you may have.

FURTHER INFORMATION

What YERVOY contains

- The active substance is ipilimumab.

Each vial contains either 50 mg or 200 mg of ipilimumab.

- The other ingredients are trometamol hydrochloride, sodium chloride, mannitol (E421), pentetic acid, polysorbate 80, sodium hydroxide, hydrochloric acid and water for injection.

What YERVOY looks like and contents of the pack

YERVOY concentrate for solution for infusion is a clear to slightly opalescent, colourless to pale yellow liquid that may contain light (few) particulates and is supplied in a glass vial with a rubber stopper sealed with aluminium.

It is available in packs containing either 1 vial of 10 mL or 1 vial of 40 mL.

Not all pack sizes may be marketed.

HOW TO STORE YERVOY

It is unlikely that you will be asked to store YERVOY yourself. It will be stored in the hospital or clinic where it is given to you.

Registration Numbers:

YERVOY (ipilimumab) concentrate solution for infusion
50mg in 10mL (5mg/mL) AUST R 174319

YERVOY (ipilimumab) concentrate solution for infusion
200mg in 40mL (5mg/mL) AUST R 174322

Date of preparation:

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