

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrYERVOY® (yur-voi)

ipilimumab for injection

Read this carefully before you start taking **YERVOY** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **YERVOY**.

Serious Warnings and Precautions

- 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 alone or in combination with nivolumab can cause serious side effects in many parts of your body which can lead to death. These serious side effects may include: inflammation of the intestines (colitis) that can cause tears or holes (perforation) in the intestines; inflammation of the liver (hepatitis) that can lead to liver failure; inflammation of the skin that can lead to severe skin reaction (toxic epidermal necrolysis or Stevens-Johnson syndrome); inflammation of the nerves that can lead to paralysis (Guillain-Barré syndrome); inflammation of hormone glands (especially the pituitary, adrenal, and thyroid glands) that may affect how these glands work; inflammation of the lung tissue (pneumonitis or interstitial lung disease); inflammation of the heart muscle (myocarditis) reducing your heart's ability to pump; inflammation of the brain (encephalitis); neuromuscular disease that leads to skeletal muscle weakness (myasthenia gravis), decreased number of red blood cells (autoimmune hemolytic anemia) and inflammation of the eyes which may lead to vision problems. Please see complete Important Safety Information for details on signs and symptoms.

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 immediately if you have, or develop, any of the symptoms listed under **Serious Side Effects, How Often They Happen and What To Do About Them**.

If you are given YERVOY in combination with OPDIVO (nivolumab), it is important that you also read the package leaflet for this medicine.

What is YERVOY used for?

Skin cancer

YERVOY (ipilimumab for injection) is a prescription medicine used to treat melanoma (a kind of skin cancer) that has spread or cannot be removed by surgery. It is for the treatment of melanoma in adults

YERVOY may be given in combination with nivolumab in adult patients with advance melanoma who have not been treated.

Kidney cancer

YERVOY may be given in combination with nivolumab in adult patients with advanced kidney cancer (called renal cell carcinoma) who have not been treated.

Lung Cancer:

YERVOY may be given in combination with nivolumab in adult patients with lung cancer who have not been treated.

YERVOY may be given in combination with nivolumab and platinum-based chemotherapy in adult patients with metastatic lung cancer (non-small cell lung cancer) who have not been treated.

Malignant Pleural Mesothelioma:

YERVOY is used in combination with nivolumab in adult patients with malignant pleural mesothelioma (a type of cancer that affects the lining of the lungs and chest wall) who have not been treated and whose tumours cannot be removed by surgery.

Esophageal Cancer:

YERVOY is used in combination with nivolumab in adult patients who test positive for PD-L1 and have a type of esophageal cancer called squamous cell carcinoma, which cannot be removed with surgery, and has come back or spread to other parts of the body.

If your doctor has prescribed YERVOY in combination with OPDIVO (nivolumab) you should read the leaflets for both medications as they contain different information.

It is not known if YERVOY is safe and effective in children less than 18 years of age.

“For the following indication(s) YERVOY has been approved with conditions (NOC/c). This means it has passed Health Canada’s review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.”

- Adults with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, when used in combination with nivolumab when your colon or rectal cancer:
 - has come back or spread
 - you have tried treatment with fluoropyrimidine-based therapy in combination with oxaliplatin or irinotecan.

“For the following indication(s) YERVOY has been approved without conditions. This means it has passed Health Canada’s review and can be bought and sold in Canada.”

- Adults with skin cancer (advanced melanoma) when used alone.
- Adults with skin cancer (advanced melanoma) when used together with nivolumab in patients who have not been treated.
- Adults with kidney cancer (advanced renal cell carcinoma) when used together with nivolumab in patients who have not been treated.
- Adults with lung cancer (advanced non-small cell cancer), if the tumour tests positive for “PD-L1”, when used together with nivolumab in patients who have not been treated.
- Adults with lung cancer (metastatic non-small cell cancer) when used together with

- nivolumab and platinum-based chemotherapy in patients who have not been treated.
- Adults with unresectable malignant pleural mesothelioma who have not been treated, when used together with nivolumab.
 - Adults with cancer of the esophagus (advanced squamous cell carcinoma) when used together with nivolumab in patients who have not been treated and who have tested positive for PD-L1.

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does YERVOY work?

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

YERVOY attaches to a target protein called cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) that can switch off the activity of cytotoxic T cells (a type of white blood cell that forms part of the immune system, the body's natural defenses). By attaching to CTLA-4, ipilimumab blocks its action and prevents it from switching off your cytotoxic T cells. This helps increase their activity against cancer cells.

YERVOY may be given in combination with OPDIVO.

OPDIVO contains the active substance nivolumab, which is a different medicine that also helps your immune system to attack and destroy cancer cells. It is important that you also read the package leaflet for this medicine. If you have any questions about nivolumab, please ask your healthcare professional.

YERVOY given with nivolumab can produce a combined effect on your immune system when taken together.

What are the ingredients in YERVOY?

Medicinal ingredients: ipilimumab

Non-medicinal ingredients: diethylene triamine pentaacetic acid (DTPA), mannitol, polysorbate 80, sodium chloride, Tris-hydrochloride, and Water for Injection. Sodium hydroxide or hydrochloric acid is added as necessary to adjust pH.

YERVOY comes in the following dosage forms:

Single use glass vials containing 50 mg/10 mL (5 mg/mL) or 200 mg/40 mL (5 mg/mL)

Do not use YERVOY if:

- are allergic to ipilimumab or any other ingredients in YERVOY

- have an active, very severe condition where your immune system attacks your body (life threatening autoimmune disease)

have received an organ transplant

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take YERVOY. Talk about any health conditions or problems you may have, including if you:

- have an active autoimmune disease, such as ulcerative colitis, Crohn's disease, lupus, or sarcoidosis
- have hepatitis
- have had an organ transplant
- take steroids or other medicines that lower your immune response
- had a severe skin reaction with a previous cancer therapy which works with your immune system
- take any medicines that stop your blood from clotting (anticoagulants)
- have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic)

Pregnancy and Breastfeeding:

- are pregnant or plan to become pregnant. You should not become pregnant while you are getting YERVOY. YERVOY can cause harm or death to your unborn baby.
- must use effective contraception while you are being treated with YERVOY and for at least 3 months after the last dose of YERVOY if you are a woman who could become pregnant.
- are breast-feeding. YERVOY may pass into your breast milk. You and your doctor should decide if you will take YERVOY or breast-feed. You should not do both.

Always update your doctor or nurse on your medical conditions.

Other warnings you should know about:

Give yourself time after taking YERVOY to see how you feel before driving a vehicle or using machinery.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Do not start a new medicine before you talk to your doctor.

The following may interact with YERVOY:

- Systemic immunosuppressants
- Anticoagulants

How to take YERVOY:

YERVOY will be given to you in a hospital or clinic under the supervision of an experienced doctor. YERVOY is a concentrate for solution for infusion. 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 saline or glucose solution before use. More than one vial may be necessary to obtain the required dose.

When YERVOY is given on its own, it will be given to you as an infusion (a drip) into a vein (intravenously) over a period of 30 minutes.

When YERVOY is given in combination with nivolumab, YERVOY is given as an infusion over 30 minutes (for the treatment of advance skin cancer or advanced kidney cancer). When YERVOY is given in combination with nivolumab and chemotherapy for the treatment of metastatic lung cancer, YERVOY is given as an infusion over 30 minutes. Nivolumab will be given on the same day (see section below for dosage and frequency of administration).

Usual dose:

- When YERVOY is given on its own, the recommended dose is 3 mg of ipilimumab per kilogram of your body weight. You will be treated with YERVOY once every 3 weeks for a total of 4 doses as tolerated, depending on your response to treatment.
- When YERVOY is given in combination with nivolumab for the treatment of advance skin cancer, the recommended dose is 3 mg of ipilimumab per kilogram of your body weight once every 3 weeks for a total of 4 doses.
- When YERVOY is given in combination with nivolumab for the treatment of advanced kidney cancer, the recommended dose is 1 mg of ipilimumab per kilogram of your body weight once every 3 weeks for a total of 4 doses.
- When YERVOY is given in combination with nivolumab for the treatment of advanced lung cancer, the recommended dose of YERVOY is 1 mg of ipilimumab per kilogram of your body weight every 6 weeks for up to 2 years.
- When YERVOY is given in combination with nivolumab and chemotherapy for the treatment of metastatic lung cancer, the recommended dose of YERVOY is 1 mg of ipilimumab per kilogram of your body weight every 6 weeks for up to 2 years. YERVOY, nivolumab and chemotherapy will be given on the same day.
- When YERVOY is given in combination with nivolumab for the treatment of unresectable malignant pleural mesothelioma, the recommended dose of YERVOY is 1 mg of ipilimumab per kilogram of your body weight every 6 weeks for up to 2 years. YERVOY and nivolumab will be given on the same day.
- When YERVOY is given in combination with nivolumab for the treatment of metastatic esophageal cancer, the recommended dose of YERVOY is 1 mg of ipilimumab per kilogram of your body weight every 6 weeks (30-minute intravenous infusion), until disease progression, unacceptable toxicity, or up to 24 months.

Please refer to the package leaflet of nivolumab and your prescribed chemotherapy in order to understand the use of these medicines. If you have questions about these medicines, please ask your healthcare professional.

Overdose:

If you think you, or a person you are caring for, have taken too much YERVOY, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed dose:

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.

What are possible side effects from using YERVOY?

These are not all the possible side effects you may have when taking YERVOY. If you experience any side effects not listed here, tell your healthcare professional.

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 most common side effects with YERVOY are loss of appetite, diarrhea, feeling sick (nausea) or being sick (vomiting), stomach pain, itching, skin rash, and feeling tired or weak.

YERVOY acts on your immune system and may cause inflammation in parts of your body. Inflammation may cause serious damage to your body and may be life threatening. Tears or holes (perforation) in the intestines, liver failure, severe skin reaction (toxic epidermal necrolysis), paralysis (Guillain-Barré syndrome) and temporary loss of sight have been reported.

It is important to tell your doctor immediately if you have any of the symptoms listed in the table below or your symptoms get worse. Your doctor can then give you treatment to prevent more severe complications. Your doctor may give you other medicines in order to reduce your symptoms, delay the next dose of YERVOY, or stop your treatment with YERVOY altogether. **Do not try to treat or diagnose symptoms yourself.** These 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 before and during treatment.

Serious side effects and what to do about them				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
COMMON	<p>Inflammation of the intestines (colitis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • diarrhea (loose stools) or more bowel movements than usual. Do not treat the diarrhea yourself. • constipation • blood in stools or dark, tarry, sticky stools • stomach pain (abdominal pain) or tenderness 		√	

Serious side effects and what to do about them				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
COMMON	Inflammation of the liver (hepatitis) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • yellowing of your skin or the whites of your eyes, • dark urine, tiredness, nausea or vomiting, loss of appetite, pain on the right side of your stomach, or bruise easily 		√	
COMMON	Inflammation of the skin <i>Symptoms may include:</i> <ul style="list-style-type: none"> • rash on your skin, mouth blisters, or peeling skin 		√	
COMMON	Inflammation of certain glands (pituitary, adrenal glands, or thyroid) so they do not make enough hormone <i>Symptoms may include:</i> <ul style="list-style-type: none"> • headaches or unusual tiredness or sleepiness • changes in behavior such as less sex drive, being irritable or forgetful, dizziness or fainting 		√	
UNCOMMON	Inflammation of the nerves <i>Symptoms may include:</i> <ul style="list-style-type: none"> • weakness of legs, arms or face • numbness or tingling in hands or feet 		√	
UNCOMMON	Inflammation in other parts of the body including eyes, kidneys, pancreas, or lung <i>Symptoms may include:</i> <ul style="list-style-type: none"> • blurry vision, double vision, cloudy vision or other vision problems including temporary loss of vision • eye pain or redness 		√	

Serious side effects and what to do about them				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
UNCOMMON	Infusion reaction <i>Symptoms may include:</i> <ul style="list-style-type: none"> • shortness of breath or trouble breathing, cough, chest tightness • dizziness, fainting, rapid or weak heartbeat • itching, hives, or feeling warm • swelling of the throat, tongue, or face • hoarse voice, throat tightness or trouble swallowing 		√	
VERY RARE	Immune Disease (Vogt-Koyanagi-Harada Syndrome) <i>Symptoms may include blurry vision, intolerance of bright light or other eye symptoms in combination with:</i> <ul style="list-style-type: none"> • neck stiffness, headache • ear ringing, difficulty hearing, dizziness, • flu-like discomfort • skin discoloration, hair loss 		√	

Graft-versus-host disease, a complication that can happen after receiving a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic), may be severe, and can lead to death, if you receive YERVOY either before or after transplant. Your healthcare provider will monitor you for the following signs and symptoms: skin rash, liver inflammation, stomach-area (abdominal) pain, and diarrhea.

If you are having a stem cell transplant, tell your transplant doctor that you have received YERVOY in the past.

Other side effects that have been reported (frequency not known) with YERVOY alone and/or YERVOY in combination with nivolumab include:

- A condition where the immune system makes too many infection fighting cells called histiocytes and lymphocytes that may cause various symptoms (haemophagocytic lymphohistiocytosis)
- A condition where your body stops producing enough new blood cells (aplastic anemia).

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

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.

Keep out of reach and sight of children.

Do not use YERVOY after the expiry date which is stated on the label and carton after EXP.

Store in a refrigerator (2°C – 8°C). Do not freeze.

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

Do not shake product.

If you want more information about YERVOY:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website [<https://www.bms.com/ca/en>], or by contacting the sponsor, Bristol-Myers Squibb Canada at: 1-866-463-6267.

This leaflet was prepared by Bristol-Myers Squibb Canada

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