

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE**  
**PATIENT MEDICATION INFORMATION**

PrOPDIVO® is used to treat:

- Adults with skin cancer (advanced melanoma) who have not been treated and who have specific mutations in a gene called BRAF.
- Adults with skin cancer (advanced melanoma) when used together with ipilimumab in patients who have not been treated.
- Adults with a type of blood cancer called classical Hodgkin Lymphoma (a type of lymphatic cancer) when the cancer has come back or spread after a type of stem cell transplant that uses your own cells (autologous), and:
  - you used the drug brentuximab vedotin, or
  - you received at least 3 kinds of treatment including an autologous stem cell transplant.
- Adults with liver cancer (hepatocellular carcinoma) when the cancer has spread or grown after treatment with sorafenib.

It has been approved for these above uses with conditions (see NOC/c below). 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.

PrOPDIVO® is used to treat:

- Adults with skin cancer (advanced melanoma) who have not been treated and who do not have a mutation in BRAF (BRAF wild-type).
- Adults with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.
- Adults with skin cancer (melanoma) to help delay or prevent the cancer from coming back after it and its metastases have been completely removed by surgery.
- Adults with lung cancer (advanced non-small cell cancer) that has spread or grown after treatment with a platinum-based chemotherapy. Patients with certain lung cancer mutations (EGFR or ALK) should only be treated with OPDIVO if their cancer grows or spreads during or after treatment with therapies targeting these mutations.
- Adults with kidney cancer (advanced renal cell carcinoma) that has spread or grown after treatment with medicines that block vessel growth (anti-angiogenic therapies).
- Adults with kidney cancer (advanced renal cell carcinoma) when used together with ipilimumab in patients who have not been treated.
- Adults with cancer of the head and neck (advanced squamous cell carcinoma) when the cancer grows or spreads on or after platinum containing chemotherapy.

It has been approved for these above uses without conditions. This means that it has passed Health Canada's review and can be bought and sold in Canada.

## **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.

**PrOPDIVO<sup>®</sup>**  
**(op-DEE-voh)**  
**nivolumab for injection 10 mg/mL**

Read this carefully before you start taking **OPDIVO** 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 **OPDIVO**.

### **What is OPDIVO used for?**

#### **Skin Cancer:**

OPDIVO<sup>®</sup> is a medicine used in adult patients to treat a type of skin cancer (melanoma) to help delay or prevent the cancer from coming back after it and its metastases have been completely removed by surgery.

OPDIVO may be given to treat a type of skin cancer that has spread or cannot be removed by surgery (advanced melanoma) in adult patients.

OPDIVO may also be given in combination with ipilimumab. It is important that you also read the package leaflet for this medicine. If you have any questions about ipilimumab, please ask your doctor.

#### **Lung Cancer:**

OPDIVO is used in adult patients to treat a type of advanced stage lung cancer (called non-small cell lung cancer) that has spread or grown after treatment with platinum containing chemotherapy.

#### **Kidney Cancer:**

OPDIVO is used in adult patients to treat advanced kidney cancer (called renal cell carcinoma) that has spread or grown after treatment with medicines that block cancer blood vessel growth.

OPDIVO may be given in combination with ipilimumab in adult patients with kidney cancer who have not been treated.

### **Head and Neck Cancer:**

OPDIVO is used in adult patients to treat advanced head and neck cancer (called squamous cell carcinoma of the head and neck) when the cancer grows or spreads on or after platinum containing chemotherapy.

### **Lymphatic cancer (classical Hodgkin Lymphoma):**

OPDIVO is used in adults with a type of blood cancer called classical Hodgkin Lymphoma (a type of lymphatic cancer) when your cancer has come back or spread after a type of stem cell transplant that uses your own stem cells (autologous), and:

- you used the drug brentuximab vedotin, or
- you received at least 3 kinds of treatment including an autologous stem cell transplant.

### **Liver Cancer**

OPDIVO is used in adult patients to treat liver cancer (called hepatocellular carcinoma) when the cancer has spread or grown after treatment with sorafenib.

### **Children:**

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

### **How does OPDIVO work?**

OPDIVO contains the active substance nivolumab which helps your immune system to attack and destroy cancer cells.

OPDIVO attaches to a target protein called programmed death-1 receptor (PD-1) that can switch off the activity of T cells (a type of white blood cell that forms part of the immune system, the body's natural defences). By attaching to PD-1, nivolumab blocks its action and prevents it from switching off your T cells. This helps increase their activity against the melanoma, lung, kidney, lymphoid, head and neck or liver cancer cells.

OPDIVO may be given in combination with YERVOY.

YERVOY contains the active substance ipilimumab, 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 ipilimumab, please ask your healthcare professional.

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

### **What are the ingredients in OPDIVO?**

The medicinal ingredient in OPDIVO is nivolumab.

The non-medicinal ingredients are hydrochloric acid, mannitol (E421), pentetic acid, polysorbate 80, sodium chloride, sodium citrate, sodium hydroxide, and water for injection.

**OPDIVO comes in the following dosage forms:**

OPDIVO comes in glass vials containing either 40 mg (in 4 mL) or 100 mg (in 10 mL) of nivolumab.

**Do not use OPDIVO if:**

you are **allergic** to nivolumab or any of the other ingredients of this medicine. **Talk to your healthcare professional** if you are not sure.

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

- **Problems with your hormone producing glands** (including the thyroid, parathyroids, pituitary, adrenal glands, and pancreas) that may affect how these glands work. Signs and symptoms that your glands are not working properly may include fatigue (extreme tiredness), weight change, headache or excessive thirst or lots of urine, decreased blood levels of calcium.
- **Diarrhea** (watery, loose or soft stools) or any symptoms of **inflammation of the intestines** (colitis), such as stomach pain and mucus or blood in stool.
- **Abnormal liver function tests.** Signs and symptoms may include eye or skin yellowing (jaundice), pain on the right side of your stomach area, or tiredness.
- **Problems with your lungs** such as breathing difficulties, or cough. These may be signs of inflammation of the lungs (pneumonitis or interstitial lung disease).
- **Abnormal kidney function tests or problems with your kidneys**, such as decreased volume of urine or inflammation of the kidneys (tubulointerstitial nephritis).
- **Had an organ transplant** (such as a kidney transplant).
- **Take other medicines that make your immune system weak.** Examples of these may include steroids, such as prednisone.

**Other warnings you should know about:**

**Tell your healthcare professional immediately** if you have any of these signs or symptoms or if they get worse. **Do not try to treat your symptoms with other medicines on your own.**

Your healthcare professional may:

- give you other medicines in order to prevent complications and reduce your symptoms,
- withhold the next dose of OPDIVO,
- or, stop your treatment with OPDIVO.

Please note that these signs and symptoms are **sometimes delayed**, and may develop weeks or months after your last dose. Before treatment, your healthcare professional will check your general health.

**Check with your healthcare professional before you are given OPDIVO if:**

- you have an autoimmune disease (a condition where the body attacks its own cells);
- you have melanoma of the eye;
- have experienced side effects with another drug, such as ipilimumab;
- have been told cancer has spread to your brain;
- or, you are on a low salt diet.

**Pregnancy and Breast-feeding:**

- you are pregnant or plan to become pregnant. You should not become pregnant while you are getting OPDIVO, OPDIVO can cause harm or death to your unborn baby.
- you must use effective contraception while you are being treated with OPDIVO and for at least 5 months after the last dose of OPDIVO if you are a woman who could become pregnant.
- you are breast-feeding. OPDIVO may pass into your breast milk. You and your doctor should decide if you will take OPDIVO or breast-feed. You should not do both.

Always update your healthcare professional on your medical conditions.

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

**How to take OPDIVO:**

You will receive treatment with OPDIVO in a hospital or clinic, under the supervision of an experienced healthcare professional.

You will get OPDIVO through an infusion (a method of putting the medicine directly into the bloodstream through a vein). It takes about 30 minutes to get a full dose.

OPDIVO is given every 2 weeks or 4 weeks, depending on the dose you are receiving. Your healthcare professional may change how often you receive OPDIVO or how long the infusion may take.

When OPDIVO is given in combination with ipilimumab, you will be given an infusion over a period of 30 minutes, every 3 weeks for the first 4 doses (combination phase). Ipilimumab will be given on the same day. Thereafter it will be given as an infusion over a period of 30 minutes, every 2 weeks or every 4 weeks, depending on the dose you are receiving (single-agent phase).

**Usual dose:**

When OPDIVO is given on its own, the recommended dose is either 3 mg of nivolumab per kilogram of your body weight every 2 weeks or 240 mg given every 2 weeks or 480 mg given

every 4 weeks. Your healthcare professional will discuss with you and help choose the appropriate dose.

When OPDIVO is given in combination with ipilimumab for the treatment of skin cancer, the recommended dose of OPDIVO is 1 mg of nivolumab per kilogram of your body weight for the first 4 doses (combination phase). Thereafter the recommended dose of OPDIVO is either 3 mg of nivolumab per kilogram of your body weight every 2 weeks or 240 mg of nivolumab given every 2 weeks or 480 mg given every 4 weeks (single-agent phase).

When OPDIVO is given in combination with ipilimumab for the treatment of advanced kidney cancer, the recommended dose of OPDIVO is 3 mg of nivolumab per kilogram of your body weight for the first 4 doses (combination phase). Thereafter the recommended dose of OPDIVO is either 3 mg of nivolumab per kilogram of your body weight every 2 weeks or 240 mg of nivolumab given every 2 weeks or 480 mg given every 4 weeks (single-agent phase).

Depending on your dose, some or all of the content of the OPDIVO 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.

**Overdose:**

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

**If you stop using OPDIVO:**

Stopping your treatment may stop the effect of the medicine. Do not stop treatment with OPDIVO unless you have discussed this with your healthcare professional.

If you have any further questions about your treatment or on the use of this medicine, ask your healthcare professional.

When OPDIVO is given in combination with ipilimumab, you will first be given OPDIVO followed by ipilimumab.

Please refer to the package leaflet of ipilimumab in order to understand the use of this medicine. If you have questions about this medicine, please ask your healthcare professional.

**Missed Dose:**

It is very important for you to keep all your appointments to receive OPDIVO. If you miss an appointment, ask your healthcare professional when to schedule your next dose.

**What are possible side effects from using OPDIVO?**

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

**Very common side effects (may affect more than 1 in 10 people):**

The most common side effects of OPDIVO when used alone are:

- Nausea
- Diarrhea
- Skin rash, itching
- Feeling tired or weak
- Decreased appetite

The most common side effects of OPDIVO when used in combination with ipilimumab are:

- Underactive thyroid gland (which can cause tiredness or weight gain), overactive thyroid gland (which can cause rapid heart rate, sweating and weight loss)
- Decreased appetite
- Headache
- Shortness of breath (dyspnea)
- 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 (arthralgia), pain in the muscles and bones (musculoskeletal pain)
- Feeling tired or weak, fever

OPDIVO acts on your immune system and may cause redness, warmth (fever), swelling and pain (inflammation) in parts of your body. This may cause serious damage to your body and some conditions may be life-threatening. You may need treatment to reduce the inflammation and OPDIVO may be stopped.

If you get any serious side effects with OPDIVO when used alone (monotherapy) or with ipilimumab (combination) (see table below), talk to your healthcare professional. Side effects may be very common (may affect more than 1 in 10 people), common (may affect less than 1 in 10 but more than 1 in 100 people), uncommon (may affect less than 1 in 100 but more than 1 in 1,000 people), or rare (may affect less than 1 in 1,000 people).

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	
<p><b>Common</b> <i>(monotherapy)</i></p> <p><b>Common to Very Common</b> <i>(combination)</i></p>	<p><b>Inflammation of the intestines (colitis)</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• diarrhea (watery, loose, or soft stools) or more bowel movements than usual. Do not treat the diarrhea yourself</li> <li>• blood or mucous in stools, or dark, tarry, sticky stools</li> <li>• stomach pain (abdominal pain) or tenderness</li> </ul>		√	
<p><b>Common</b> <i>(monotherapy)</i></p> <p><b>Very Common</b> <i>(combination)</i></p>	<p><b>Inflammation of the thyroid, adrenal or pituitary glands</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• headaches that will not go away or unusual</li> <li>• unusual tiredness or sleepiness</li> <li>• weight changes (weight gain or weight loss)</li> <li>• changes in mood or behaviour such as less sex drive, being irritable or forgetful, or depression</li> <li>• dizziness or fainting</li> </ul>		√	



<b>Serious side effects and what to do about them</b>				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
<p><b>Uncommon</b> <i>(monotherapy)</i></p> <p><b>Common</b> <i>(combination)</i></p>	<p><b>Inflammation of the liver (hepatitis)</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• extreme tiredness</li> <li>• yellowing of your skin (jaundice) or the whites of your eyes</li> <li>• severe nausea or vomiting</li> <li>• pain on the right side of your stomach (abdomen)</li> <li>• bruise easily</li> </ul>		√	
<p><b>Uncommon</b> <i>(monotherapy, combination)</i></p>	<p><b>Inflammation of the kidney (nephritis)</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• changes in urine output (increase or decrease)</li> <li>• dark urine (tea-coloured)</li> <li>• swelling of extremities</li> </ul>		√	
<p><b>Common</b> <i>(monotherapy, combination)</i></p>	<p><b>Inflammation of the lung (pneumonitis)</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• trouble breathing, shortness of breath</li> <li>• cough (new or worsening) with or without mucus</li> </ul>		√	
<p><b>Uncommon</b> <i>(monotherapy, combination)</i></p>	<p><b>Eye problems</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• changes in eyesight</li> <li>• eye pain or redness</li> <li>• blurred or blurry vision, or other vision problems</li> </ul>		√	

<b>Serious side effects and what to do about them</b>				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
<p><b>Uncommon</b> <i>(monotherapy)</i></p> <p><b>Uncommon to common</b> <i>(combination)</i></p>	<p><b>Blood sugar problems (diabetes or ketoacidosis)</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• hunger or excessive thirst</li> <li>• need to urinate more often</li> <li>• increased appetite with weight loss, or loss of appetite</li> <li>• muscle weakness</li> <li>• sleepiness or drowsiness</li> <li>• depression</li> <li>• irritability</li> <li>• feeling unwell</li> </ul>		√	
<p><b>Common</b> <i>(monotherapy, combination)</i></p>	<p><b>Inflammation of the skin (severe skin problems)</b> <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> <li>• severe skin reactions or rash</li> <li>• itching</li> <li>• skin blistering and peeling</li> <li>• ulcers in the mouth or other mucous membranes</li> <li>• raised skin lumps/bumps (skin nodules)</li> <li>• dry skin</li> </ul>		√	

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	
<b>Uncommon</b> <i>(monotherapy, combination)</i>	<b>Inflammation of the brain (encephalitis)</b> <i>Symptoms may include:</i> <ul style="list-style-type: none"> <li>• headache</li> <li>• fever</li> <li>• confusion</li> <li>• memory problems</li> <li>• sleepiness or drowsiness</li> <li>• seeing things that are not really there (hallucinations)</li> <li>• seizures (fits)</li> <li>• stiff neck</li> </ul>		√	
<b>Rare</b> <i>(monotherapy, combination)</i>	<b>Inflammation of the muscles (myositis), inflammation of the heart muscle (myocarditis), or breakdown of skeletal muscle (rhabdomyolysis):</b> <i>Symptoms may include:</i> <ul style="list-style-type: none"> <li>• muscle or joint pain, stiffness, or weakness</li> <li>• chest pain, irregular heartbeat, or palpitations</li> <li>• confusion or memory problems</li> <li>• severe fatigue</li> <li>• difficulty walking</li> </ul>		√	
<b>Rare</b> <i>(monotherapy, combination)</i>	<b>Problems with other organs</b> <i>Symptoms may include:</i> <ul style="list-style-type: none"> <li>• loss of nerve function or sensation of paralysis</li> <li>• swollen lymph nodes</li> <li>• numbness or tingling in hands or feet</li> <li>• swelling in extremities</li> <li>• abdominal pain, nausea or vomiting (pancreatitis)</li> <li>• indigestion or heartburn</li> </ul>		√	

**Severe infusion reactions** may occur (uncommon: less than 1 in 100 but more than 1 in 1,000). Symptoms may include chills or shaking, itching or rash, flushing, difficulty breathing, dizziness, fever, or feeling like passing out.

**Complications of stem cell transplant that uses donor stem cells (allogeneic) after treatment with OPDIVO.** These complications can be severe and can lead to death. Your healthcare professional will monitor you for signs of complications if you have an allogeneic stem cell transplant. If you are having a stem cell transplant, tell your transplant doctor that you have received OPDIVO in the past.

Also tell your healthcare professional before you are given OPDIVO if you have received an allogeneic stem cell transplant.

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

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

A condition where the immune system makes too many infection fighting cells called histiocytes and lymphocytes that may cause various symptoms (haemophagocytic lymphohistiocytosis).

### **Changes in test results**

OPDIVO may cause changes in the results of tests carried out by your healthcare professional. These include:

- Abnormal liver function tests (increased amounts of the liver enzymes aspartate aminotransferase, alanine aminotransferase or alkaline phosphatase in your blood, higher blood levels of bilirubin).
- Abnormal kidney function tests (increased amounts of creatinine in your blood).
- 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.
- Increased or decreased amount of calcium or potassium.
- Increased or decreased blood levels of magnesium or sodium.

**Tell your healthcare professional immediately** if you get any of the side effects listed above. Do not try to treat your symptoms with other medicines on your own.

### **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 \(https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html\)](https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.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 OPDIVO 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 OPDIVO after the expiry date which is stated on the label and carton after EXP.

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

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

### **If you want more information about OPDIVO:**

- 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](#); the manufacturer's website at:
- <https://www.bms.com/ca/en>  
or by contacting the sponsor, Bristol-Myers Squibb Canada Co. at: 1-866-463-6267.

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