Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

(op-DEE-voh)
PrOPDIVO®
nivolumab for injection 10 mg/mL

This Patient Medication Information is written for the person who will be taking OPDIVO. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have questions or want more information about OPDIVO, or the condition this medication is treating, talk to a healthcare professional.

Serious warnings and precautions box

Opdivo 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.

Opdivo given alone or in combination with ipilimumab can cause serious side effects in parts of your body which can lead to death. These serious side effects may include: inflammation of the lungs (pneumonitis or interstitial lung disease), inflammation of the brain (encephalitis), inflammation of the heart muscle (myocarditis), inflammation of the skin (severe skin problems), and decreased number of red blood cells (autoimmune hemolytic anemia).

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 healthcare professional immediately if you have, or develop, any of the symptoms listed under the section "*What are possible side effects from using Opdivo and Serious Side Effects and What to do About Them*."

If you are given Opdivo in combination with ipilimumab, it is important that you also read the package leaflet for this medicine.

What Opdivo is used for:

Skin Cancer:

Opdivo® 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 (melanoma) after complete removal by surgery in adult patients (treatment after surgery is called adjuvant therapy).

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.

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

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

Opdivo may be given in combination with chemotherapy that contains platinum and another chemotherapy medicine before you have surgery for your lung cancer (non-small cell lung cancer). Treatment prior to surgery is called neoadjuvant therapy.

Malignant Pleural Mesothelioma:
Opdivo is used in combination with ipilimumab 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.

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 advanced kidney cancer who have not been treated.

Opdivo may also be given in combination with cabozantinib in adult patients with advanced kidney cancer that cannot be treated with radiation or surgery or disease that is metastatic, and who have not been treated. It is important that you also read the package leaflet for cabozantinib. If you have any questions about cabozantinib, please ask your doctor.

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.

Colon or Rectal Cancer:

Opdivo in combination with ipilimumab is used in adults for the first treatment of colon or rectal cancer that cannot be removed with surgery, or has spread to other parts of the body and is shown by a laboratory test to be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

Opdivo in combination with ipilimumab is used in adults for the treatment of colon or rectal cancer that is shown by a laboratory test to be MSI-H or dMMR, and:

- you used the drug fluoropyrimidine in combination with oxaliplatin, or irinotecan and the cancer has spread or grown or you are no longer tolerating the treatment

Esophageal or Gastroesophageal Junction Cancer:

Esophageal cancer is cancer of the esophagus, the tube that connects your throat to your stomach. Gastroesophageal junction (GEJ) cancer is cancer of the junction between the esophagus and the stomach.

Opdivo is used in adult patients who have been treated with chemoradiation followed by surgery to remove the cancer.

Opdivo is also used 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.

Cancer of the stomach, esophagus or the junction between the stomach and esophagus (gastric, esophageal, or gastroesophageal junction cancers):

Opdivo may be used in combination with chemotherapy that contains fluoropyrimidine and platinum when your gastric, gastroesophageal junction or esophageal cancer:

- is a type called adenocarcinoma, and
- cannot be removed with surgery

Bladder and Urinary Tract Cancers:

Opdivo is used in adult patients to help prevent cancer of the urinary tract from coming back after it was removed by surgery.

Opdivo may be used in combination with chemotherapy medicines cisplatin and gemcitabine as your first treatment when your urinary tract cancer (urothelial carcinoma) has spread to other parts of the body (metastatic) or cannot be removed by surgery.

Liver Cancer (hepatocellular carcinoma):

Opdivo is used in adult patients to help remove cancer of the liver.

Opdivo is used in combination with ipilimumab as your first line treatment when your liver cancer cannot be removed with surgery (advanced) or has spread to other parts of the body (metastatic).

Children:

It is not known if Opdivo is safe and effective in children less than 18 years of age. Therefore, Health Canada has not authorized an indication for children less than 18 years of age.

For the following indication(s) Opdivo 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 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 microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, when used in combination with ipilimumab 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.
- Adults with bladder or urinary tract cancer at high risk of recurrence when the cancer was removed by surgery and you may have received chemotherapy that contains platinum prior to surgery.

For the following indication(s) Opdivo 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 or when used together with ipilimumab in patients who have not been treated.
- 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 skin cancer (melanoma) after complete removal by surgery (adjuvant therapy).
- 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 lung cancer (advanced non-small cell cancer), if the tumour tests positive for "PD-L1", when used together with ipilimumab in patients who have not been treated.
- Adults with lung cancer (metastatic non-small cell cancer) when used together with ipilimumab and platinum-based chemotherapy in patients who have not been treated.
- Adults with lung cancer (non-small cell cancer) in combination with chemotherapy before surgery.
- Adults with unresectable malignant pleural mesothelioma who have not been treated, when used together with ipilimumab.
- 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 kidney cancer (advanced renal cell carcinoma) when used together with cabozantinib 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.
- Adults with cancer of the esophagus or junction between the esophagus and the stomach [gastroesophageal junction (GEJ)] who have been treated with chemoradiation followed by surgery to remove the cancer.
- Adults with gastric, gastroesophageal junction or esophageal adenocarcinoma (stomach and gullet cancer).
- Adults with cancer of the esophagus (advanced squamous cell carcinoma) when used together with chemotherapy or when used together with ipilimumab in patients who have not been treated and who have tested positive for PD-L1.

- Adults with cancer of the urinary tract (urothelial carcinoma) in combination with cisplatin and gemcitabine chemotherapies as a first treatment for cancer that cannot be removed by surgery or has spread to other parts of the body (unresectable or metastatic).
- Adults with cancer of the liver (hepatocellular carcinoma) when used together with ipilimumab as a first line treatment for cancer that cannot be removed by surgery or has spread to other parts of the body (unresectable or advanced).
- Adults with MSI-H or dMMR metastatic colorectal cancer, when used in combination with ipilimumab, who have not been treated and your colon or rectal cancer has spread to other parts of the body.

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 Opdivo works:
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, liver, colon, rectal or stomach and gullet cancer cells.

Opdivo may be given in combination with ipilimumab.

Ipilimumab 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 ipilimumab can produce a combined effect on your immune system when taken together.

Opdivo may be given in combination with cabozantinib. Please refer to the package leaflet of cabozantinib in order to understand the use of this medicine. If you have questions about this medicine, please ask your doctor.

Opdivo may be given in combination with chemotherapy. Please refer to the package leaflets for the chemotherapy medicines in order to understand their use. If you have questions about the chemotherapy medicines given with Opdivo, please ask your healthcare professional.

The ingredients in Opdivo are:
Medicinal ingredient: nivolumab.

Non-medicinal ingredients: 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, solution for IV injection, 10 mg nivolumab/mL, 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 if you have:

- **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.
- If you are pregnant or plan to become pregnant.
- If you are breast-feeding.

Other warnings you should know about:

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

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 Opdivoif 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.

It is important that you also read the package leaflet for ipilimumab and if you have any questions, please ask your doctor. **Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

The following may interact with Opdivo:

No drug-drug interaction studies have been conducted with nivolumab.

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, 3 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.

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 every 3 weeks, and ipilimumab is given every 3 weeks on the same day as Opdivo, 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 or with a previously treated type of colon or rectal cancer (colorectal cancer), the recommended dose of Opdivo is 3 mg of nivolumab per kilogram of your body weight every 3 weeks, and ipilimumab is given every 3 weeks on the same day as Opdivo, 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 as a first treatment of colon or rectal cancer, the recommended dose of Opdivo is 240 mg of nivolumab every 3 weeks, and 1 mg/kg ipilimumab is given every 3 weeks on the same day as Opdivo, for the first 4 doses (combination phase). Thereafter the recommended dose of Opdivo is either 240 mg of nivolumab every 2 weeks or 480 mg of nivolumab given every 4 weeks (single-agent phase).
- When Opdivo is given in combination with cabozantinib for the treatment of advanced kidney cancer, the recommended dose of Opdivo is 240 mg of nivolumab every 2 weeks, or 480 mg every 4 weeks and cabozantinib 40 mg is given once daily by mouth.
- When Opdivo is given in combination with ipilimumab for the treatment of advanced lung cancer, the recommended dose of Opdivo is 3 mg of nivolumab per kilogram of your body weight every 2 weeks or 360 mg every 3 weeks, and ipilimumab is given every 6 weeks, for up to 2 years.
- When Opdivo is given in combination with ipilimumab and chemotherapy for the treatment of metastatic lung cancer, the recommended dose of Opdivo is 360 mg of nivolumab every 3 weeks, and ipilimumab is given every 6 weeks, for up to 2 years. Chemotherapy is given every 3 weeks for the first 2 cycles only. Opdivo, ipilimumab and chemotherapy will be given on the same day.
- When Opdivo is given in combination with chemotherapy before surgery for non-small cell lung cancer, the recommended dose of Opdivo is 360 mg every 3 weeks for 3 cycles only. Opdivo and chemotherapy will be given on the same day.
- When Opdivo is given in combination with ipilimumab for the treatment of unresectable malignant pleural mesothelioma, the recommended dose of Opdivo is 3 mg of nivolumab per kilogram of your body weight every 2 weeks or 360 mg of nivolumab every 3 weeks, and ipilimumab is given every 6 weeks, for up to 2 years. Opdivo and ipilimumab will be given on the same day.
- When Opdivo is given in combination with chemotherapy for the treatment of advanced gastric, gastroesophageal junction or esophageal adenocarcinoma cancer, the recommended dose of Opdivo is 240 mg of nivolumab every 2 weeks or 360 mg of nivolumab every 3 weeks. Opdivo and chemotherapy will be given on the same day.
- When Opdivo is given in combination with ipilimumab for the treatment of metastatic esophageal cancer, the recommended dose of Opdivo is 3mg/kg Q2W (30-minute intravenous

infusion) or 360 mg Q3W (30-minute intravenous infusion) with ipilimumab 1 mg/kg Q6W (30-minute intravenous infusion), until disease progression, unacceptable toxicity, or up to 24 months.

- When Opdivo is given in combination with chemotherapy for the treatment of metastatic esophageal cancer, the recommended dose of Opdivo is 240 mg Q2W (30-minute intravenous infusion) or 480 mg Q4W (30-minute intravenous infusion) in combination with fluoropyrimidine- and platinum-based chemotherapy, until disease progression, unacceptable toxicity, or up to 24 months.

- When Opdivo is given in combination with cisplatin and gemcitabine chemotherapies for the treatment of unresectable or metastatic urothelial carcinoma, the recommended dose of Opdivo is 360 mg every 3 weeks for up to 6 cycles followed by Opdivo monotherapy at either 240 mg every 2 weeks or at 480 mg every 4 weeks, until disease progression, unacceptable toxicity, or up to 24 months.
- When Opdivo is given in combination with ipilimumab for the treatment of liver cancer, the recommended dose of Opdivo is 1 mg of nivolumab per kilogram of your body weight every 3 weeks, and ipilimumab is given every 3 weeks on the same day as Opdivo, for the first 4 doses (combination phase). Thereafter the recommended dose of Opdivo is either 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:

If you think you, or a person you are caring for, have taken too much Opdivo, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or 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 and chemotherapy, or with chemotherapy you will first be given Opdivo followed by ipilimumab (if applicable) and then by chemotherapy.

Please refer to the package leaflet of ipilimumab 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.

When Opdivo is given in combination with cabozantinib, you will first be given Opdivo followed by cabozantinib.

Please refer to the package leaflet of cabozantinib 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.

Possible side effects from using Opdivo:

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

Very common side effects (may affect more than 1 in 10 people):
When Opdivo is used alone:

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

When Opdivo is used in combination with ipilimumab:

- 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

When Opdivo is used in combination with cabozantinib:

- Feeling tired
- rash
- diarrhea
- nausea
- change in sense of taste
- pain in muscles, bones and joints

- upper respiratory tract infection
- a skin condition called hand-foot syndrome
- stomach-area (abdominal) pain
- decreased appetite
- low thyroid hormone levels (hypothyroidism)
- liver problems
- high blood pressure (hypertension)

When Opdivo is used in combination with ipilimumab and chemotherapy:

- Nausea
- Diarrhea
- Vomiting
- Skin rash sometimes with blisters, itching
- Feeling tired or weak
- Underactive thyroid gland (which can cause tiredness or weight gain)
- Decreased appetite
- Decrease in the number of red blood cells (which can make you feel tired or become short of breath)
- Decrease in the number of white blood cells (which can increase your chance for infection)

When Opdivo is used in combination with chemotherapy:

- numbness, pain, tingling, and/or burning along the nerves
- nausea
- low white blood cells (neutropenia)
- feeling tired
- low red blood cells (anemia)
- diarrhea
- low platelet count (thrombocytopenia)
- vomiting
- decreased appetite
- stomach-area (abdominal) pain
- constipation
- changes in liver function tests
- pain in muscles, bones and joints
- rash

- malaise
- anemia
- alopecia
- hiccups
- neuropathy peripheral
- Itchy skin
- low thyroid hormone levels (hypothyroidism)
- changes in kidney function tests

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 in combination with ipilimumab or ipilimumab and chemotherapy or chemotherapy (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 this drug and get immediate medical help
		Only if severe	In all cases	
COMMON *(monotherapy)* **COMMON TO VERY COMMON** *(combination)*	**Inflammation of the intestines (colitis)** *Symptoms may include:* • diarrhea (watery, loose, or soft stools) or more bowel movements than usual. Do not treat the diarrhea yourself • blood or mucous in stools, or dark, tarry, sticky stools • stomach pain (abdominal pain) or tenderness		**√**	

COMMON *(monotherapy)* **VERY COMMON** *(combination)*	**Inflammation of the thyroid, adrenal or pituitary glands** *Symptoms may include:* • headaches that will not go away or unusual • unusual tiredness or sleepiness • weight changes (weight gain or weight loss) • changes in mood or behaviour such as less sex drive, being irritable or forgetful, or depression • dizziness or fainting		**√**	
UNCOMMON *(monotherapy)* **COMMON** *(combination)*	**Inflammation of the liver (hepatitis)** *Symptoms may include:* • extreme tiredness • yellowing of your skin (jaundice) or the whites of your eyes • severe nausea or vomiting • pain on the right side of your stomach (abdomen) • bruise easily		**√**	
UNCOMMON *(monotherapy, combination)*	**Inflammation of the kidney (nephritis)** *Symptoms may include:* • changes in urine output (increase or decrease) • dark urine (tea-coloured) • swelling of extremities		**√**	
COMMON *(monotherapy, combination)*	**Inflammation of the lung (pneumonitis)** *Symptoms may include:* • trouble breathing, shortness of breath • cough (new or worsening) with or without mucus		**√**	

UNCOMMON *(monotherapy, combination)*	**Eye problems** *Symptoms may include:* • changes in eyesight • eye pain or redness • blurred or blurry vision, or other vision problems		**√**	
UNCOMMON *(monotherapy)* **UNCOMMON TO COMMON** *(combination)*	**Blood sugar problems (diabetes or ketoacidosis)** *Symptoms may include:* • hunger or excessive thirst • need to urinate more often • increased appetite with weight loss, or loss of appetite • muscle weakness • sleepiness or drowsiness • depression • irritability • feeling unwell		**√**	
COMMON *(monotherapy, combination)*	**Inflammation of the skin (severe skin problems)** *Symptoms may include:* • severe skin reactions or rash • itching • skin blistering and peeling • ulcers in the mouth or other mucous membranes • raised skin lumps/bumps (skin nodules) • dry skin		**√**	
UNCOMMON *(combination)*	**Inflammation of the skin (severe skin problems)** *Symptoms may include:* changes in any area of the skin and/or genital area that are associated with drying out, thinning, itching and pain (other lichen disorders)		**√**	

UNCOMMON *(monotherapy, combination)*	**Inflammation of the brain (encephalitis)** *Symptoms may include:* • headache • fever • confusion • memory problems • sleepiness or drowsiness • seeing things that are not really there (hallucinations) • seizures (fits) • stiff neck		**√**	
UNCOMMON *(monotherapy, combination)*	**Inflammation of the nerves (demyelination)** *Symptoms may include:* • muscle weakness • muscle stiffness • numbness • loss of reflexes • uncoordinated movements		**√**	
UNCOMMON *(monotherapy, combination)*	**Muscle weakness (myasthenia gravis or myasthenic syndrome**) *Symptoms may include:* • difficulty walking and climbing stairs • difficulty lifting objects or raising the arms • drooping eyelids • chewing or swallowing problems		**√**	

RARE *(monotherapy, combination)*	**Inflammation of the muscles (myositis), inflammation of the heart muscle (myocarditis), or breakdown of skeletal muscle (rhabdomyolysis):** *Symptoms may include:* • muscle or joint pain, stiffness, or weakness • chest pain, irregular heartbeat, or palpitations • confusion or memory problems • severe fatigue • difficulty walking		**√**	
RARE *(monotherapy, combination)*	**Problems with other organs** *Symptoms may include:* • loss of nerve function or sensation of paralysis • swollen lymph nodes • numbness or tingling in hands or feet • swelling in extremities • abdominal pain, nausea or vomiting (pancreatitis) • indigestion or heartburn		**√**	
RARE *(monotherapy, combination)*	**Inflammation of the spinal cord (myelitis and transverse myelitis)** *Symptoms may include:* • Pain, numbness, tingling, or weakness in the arms, legs or torso • Bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating and constipation		**√**	

Other serious 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).
- A condition where the immune system mistakenly destroys red blood cells (oxygen carrying cells) and results in decreased number of red blood cells (autoimmune hemolytic anemia).
- A condition where your body stops producing enough new blood cells (aplastic anemia).

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.

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.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 (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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