PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrOPDUALAG™

(op-DEW-uh-lag)

nivolumab and relatlimab for injection

Read this carefully before you start taking **OPDUALAG** 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 **Opdualag**.

Serious Warnings and Precautions

Opdualag 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.

Opdualag 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), acute lung swelling caused by too much fluid trapped (edema) and a rare disease in which your immune system makes too many of otherwise normal infection fighting cells called histiocytes and lymphocytes (Haemophagocytic lymphohistiocytosis). These are not all of the possible serious or life-threatening side effects you may experience with Opdualag (see *"Serious side effects and what to do about them"*)

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 Opdualag and Serious Side Effects and What to do About Them*."

If you are given Opdualag, it is important that you also read the package leaflet of Opdivo (nivolumab) since it is a component of Opdualag, and serious and life-threatening side effects have been observed with nivolumab.

What is Opdualag used for?

- Opdualag is a medicine used to treat melanoma (a type of skin cancer) that has spread to other parts of the body or that cannot be removed with surgery, in adults and in children who are at least 12 years of age.

How does Opdualag work?

Opdualag contains two active substances: nivolumab and relatlimab, which are monoclonal antibodies. They are designed to recognise and attach to a specific target substance in the body.

Nivolumab attaches to a target protein called programmed death-1 receptor (PD-1). Relatlimab attaches to a target protein called lymphocyte activation gene-3 (LAG-3). Those proteins 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 and LAG-3, nivolumab and relatlimab block the actions of these two proteins and prevent them from switching off your T cells. This helps increase the T cell activity against the melanoma cancer cells.

What are the ingredients in Opdualag?

Medicinal ingredients: nivolumab and relatlimab.

Non-medicinal ingredients: histidine, histidine hydrochloride monohydrate, pentetic acid, polysorbate 80, sucrose and water for injection.

Opdualag comes in the following dosage forms:

One vial of 20 mL contains 240 mg of nivolumab and 80 mg of relatlimab. Each mL of concentrate for solution for infusion (sterile concentrate) contains 12 mg of nivolumab and 4 mg of relatlimab.

Opdualag is a clear to opalescent, colourless to slightly yellow liquid that is essentially free of particles.

It is available in cartons containing one glass vial.

Do not use Opdualag if:

- you are allergic to nivolumab, relatlimab or any of the other ingredients of this medicine. Talk to your healthcare professional if you are not sure.
- you are younger than 12 years of age or you are 12 years of age or older and weigh less than 40 kg.

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

- **Problems with your lungs** such as breathing difficulties or cough. These may be signs of inflammation of the lungs (pneumonitis or interstitial lung disease).
- **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.
- **Inflammation of the liver (hepatitis).** Signs and symptoms of hepatitis may include abnormal liver function tests, eye or skin yellowing (jaundice), pain on the right side of your stomach area, or tiredness.
- **Inflammation or problems with your kidneys.** Signs and symptoms may include abnormal kidney function tests, or decreased volume of urine.
- **Problems with your hormone producing glands** (including the pituitary, the thyroid and adrenal glands) that may affect how these glands work. Signs and symptoms that these glands are not working properly may include fatigue (extreme tiredness), weight change or headache and visual disturbances.
- **Diabetes** including a serious, sometimes life-threatening problem due to acid in the blood produced from diabetes (**diabetic ketoacidosis**); symptoms may include feeling more hungry or thirsty than usual, need to urinate more often, weight loss, feeling tired or having difficulty thinking clearly, breath that smells sweet or fruity, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat, feeling sick or being sick, stomach pain, and deep or fast breathing.
- **Inflammation of the skin** that can lead to severe skin reactions (known as toxic epidermal necrolysis and Stevens-Johnson syndrome). Signs and symptoms of severe skin reactions may include rash, itching, and peeling of the skin (possibly fatal).
- **Inflammation of the heart muscle** (myocarditis). Signs and symptoms may include chest pain, irregular and/or rapid heartbeat, fatigue, swelling in the ankles or shortness of breath.
- **Solid organ transplant rejection.**

- **Haemophagocytic lymphohistiocytosis**. A rare disease in which your immune system makes too many of otherwise normal infection fighting cells called histiocytes and lymphocytes. Symptoms may include enlarged liver and/or spleen, skin rash, lymph node enlargement, breathing problems, easy bruising, kidney abnormalities, and heart problems.
- **Graft-versus-host disease** after blood stem cell transplantation (where the transplanted cells from a donor attack your own cells). If you have received one of these transplants, your healthcare professional will consider whether you should receive treatment with Opdualag. Graft-versus-host disease can be severe and can lead to death.
- **Infusion reactions** which may include shortness of breath, itching or rash, dizziness or fever.

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 Opdualag,
- or stop your treatment with Opdualag altogether.

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. You will also have **blood tests** during your treatment.

Check with your healthcare professional or nurse before you are given Opdualag if:

- you have an active **autoimmune disease** (a condition where the body attacks its own cells);
- you have **melanoma of the eye**;
- you have been told that your **cancer has spread to your brain**;
- you have been taking **medicines to suppress your immune system**.

Other warnings you should know about:

Pregnancy and breast-feeding
Before starting Opdualag, tell your healthcare professional if you are pregnant or think you might be, if you are planning to become pregnant, or if you are breast-feeding.

Opdualag can cause harm or death to your unborn baby. You must use effective contraception while you are being treated with Opdualag and for at least 5 months following the last dose of Opdualag if you are a woman who could become pregnant.

Opdualag may pass into your breast milk. Do not breast-feed during treatment with Opdualag and for at least 5 months after your last dose of Opdualag.

Driving and using machines
Opdualag may have an influence on your ability to drive and use machines, so you should; use caution when performing these activities until you are sure that Opdualag does not adversely affect you.

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 Opdualag:

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

Before you are given Opdualag, tell your healthcare professional if you are taking any medicines that suppress your immune system, such as corticosteroids, since these medicines may interfere with the effect of Opdualag. However, once you are treated with Opdualag, your healthcare professional may give you corticosteroids to reduce any possible side effects that you may have during your treatment. **Tell your healthcare professional** if you are taking or have recently taken any other medicines. **Do not take any other medicines** during your treatment without talking to your healthcare professional first.

How to take Opdualag:

- You will receive treatment with Opdualag in a hospital or clinic, under the supervision of an experienced healthcare professional.
- Your healthcare professional will give you Opdualag into your vein through an intravenous (IV) line over 30 minutes.
- Opdualag is usually given every 4 weeks. Your healthcare provider will decide how many treatments you need.
- Your healthcare professional will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare professional as soon as possible to reschedule your appointment.

Usual dose:

The recommended dose for Adults and Pediatric patients 12 years of age or older who weigh at least 40 kg is:

- Opdualag (480 mg nivolumab and 160 mg relatlimab) every 4 weeks.

Depending on your dose, the appropriate amount of Opdualag may be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection or glucose 50 mg/mL (5%) solution for injection before use. More than one vial of Opdualag may be necessary to obtain the required dose.

Overdose:

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

If you stop using Opdualag:

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

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

Missed Dose:

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

What are possible side effects from using Opdualag?

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

Be aware of important symptoms of inflammation. Opdualag 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 and need treatment or withdrawal of Opdualag.

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

- infection of the urinary tract
- decreased number of red blood cells (which carry oxygen) and white blood cells (lymphocytes, neutrophils, leucocytes) (which are important in fighting infection)
- underactive thyroid gland (which can cause tiredness or weight gain)
- decreased appetite
- headache
- difficulty breathing; cough
- diarrhea (watery, loose or soft stools); nausea; stomach pain; constipation
- skin rash, sometimes with blisters; skin colour change in patches (vitiligo); itching
- pain in the muscles, bones and joints
- feeling tired or weak; fever.

Changes in the results of tests carried out by your healthcare professional may show:

- abnormal liver function (increased amounts of the liver enzymes alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase in your blood)
- abnormal kidney function (increased amounts of creatinine in your blood)
- decrease of sodium, magnesium and increase of potassium and decrease or increase of calcium in your blood.

Common side effects (may affect more than 1 in 100 people and up to 1 in 10 people)

- infections of the upper respiratory tract
- decreased number of platelets (cells which help the blood to clot); increase in some white blood cells
- decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys); inflammation of the pituitary gland situated at the base of the brain; overactive thyroid gland; inflammation of the thyroid gland;
- diabetes; low sugar levels in the blood; weight loss; high uric acid levels in the blood; decreased levels of albumin in the blood; dehydration
- state of confusion
- inflammation of the nerves (causing numbness, weakness, tingling or burning pain of the arms and legs); dizziness; changes in the sense of taste
- inflammation of the eye (which causes pain and redness, vision problems or blurry vision); vision problems, dry eyes, abnormal or excessive tears
- inflammation of the heart muscle
- inflammation of a vein, which can cause redness, tenderness and swelling
- inflammation of the lungs (pneumonitis), characterised by coughing and difficulty breathing; nasal congestion
- inflammation of the intestines (colitis); inflammation of the pancreas; inflammation of the stomach (gastritis); difficulty in swallowing; mouth ulcers and cold sores; dry mouth
- inflammation of the liver (hepatitis)
- unusual hair loss or thinning (alopecia); isolated area of skin growth that becomes red and itchy (lichenoid keratosis); sensitivity to light; dry skin

- painful joints (arthritis); muscle spasms; muscle weakness
- kidney failure; high levels of proteins in the urine
- edema (swelling); flu-like symptoms; chills
- reactions related to the administration of the medicine.

Changes in the results of tests carried out by your healthcare professional may show:

- abnormal liver function (higher blood levels of the waste product bilirubin; higher blood levels of the liver enzyme gamma-glutamyl transferase)
- increase in sodium and magnesium
- increased level of troponin (a protein released into the blood when the heart is damaged)
- increased level of the enzyme that breaks down glucose (sugar), the enzyme that breaks down fats, the enzyme that breaks down starch

Uncommon side effects (may affect up to 1 in 100 people)

- inflammation and infection in the hair follicles
- disorder in which red blood cells are destroyed faster than they can be made
- underactive function of the pituitary gland situated at the base of the brain; underactive function of the glands producing sex hormones
- inflammation of the brain, which may include confusion, fever, memory problems or seizures (encephalitis); a temporary inflammation of the nerves that causes pain, weakness, and paralysis in the extremities (Guillain-Barré syndrome); inflammation of the optic nerve that may cause a complete or partial loss of vision
- an inflammatory disorder, most likely of autoimmune origin, affecting the eyes, skin and the membranes of the ears, brain and spinal cord (Vogt-Koyanagi-Harada syndrome); increase blood congestion in the eye
- fluid around the heart
- asthma
- inflammation of the food pipe
- inflammation of the bile duct
- skin rashes and blistering on the legs, arms and abdomen (pemphigoid); skin disease with thickened patches of red skin, often with silvery scales (psoriasis); hives (itchy, bumpy rash)
- inflammation of the muscles causing weakness, swelling, and pain; 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 muscles causing pain or stiffness; inflammation of the joints (painful joint disease); disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs, such as joints, skin, brain, lungs, kidneys, and blood vessels (systemic lupus erythematosus)
- inflammation of the kidney
- absence of sperm in the semen.

Changes in the results of tests carried out by your healthcare professional may show:

- abnormal c-reactive protein increased
- red blood cell sedimentation rate increased.

If you get any serious side effects with Opdualag, 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**	
COMMON			
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 • stool that are black, tarry, sticky, or have blood or mucus • stomach pain (abdominal pain) or tenderness		√	
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 or bleeding		√	
Inflammation of the lung (pneumonitis) *Symptoms may include:* • trouble breathing, shortness of breath • cough (new or worsening) with or without mucus • chest pain		√	
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 nose, throat, or genital area • raised skin lumps/bumps (skin nodules)		√	
Inflammation of the thyroid, adrenal or pituitary glands *Symptoms may include:* • headaches that will not go away or unusual		√	

• unusual tiredness or sleepiness • eye sensitivity to light • eye problems • rapid heartbeat • increased sweating • extreme tiredness • feeling more hungry or thirsty than usual • urinating more often than usual • hair loss • feeling cold • constipation • your voice gets deeper • 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			
Inflammation of the heart muscle (myocarditis) • new or worsening chest pain • palpitations • shortness of breath • fatigue • swelling in ankles		√	
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		√	
Inflammation of the nerves *Symptoms may include:* • muscle weakness • muscle stiffness • numbness • loss of reflexes • uncoordinated movements		√	

Inflammation of the eye *Symptoms may include:* • changes in eyesight • eye pain or redness • blurred or blurry vision, or other vision problems		√	
UNCOMMON			
Inflammation of the kidney (nephritis) *Symptoms may include:* • changes in urine output (increase or decrease) • blood in the urine or dark urine (tea-coloured) • swelling of ankles • loss of appetite		√	
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		√	
Inflammation of the muscles (myositis): *Symptoms may include:* • muscle or joint pain, stiffness, or weakness		√	

Other serious side effects include:

Haemophagocytic lymphohistiocytosis. A rare disease in which your immune system makes too many of otherwise normal infection fighting cells called histiocytes and lymphocytes. Symptoms may include enlarged liver and/or spleen, skin rash, lymph node enlargement, breathing problems, easy bruising, kidney abnormalities, and heart problems.

Severe infusion reactions may occur (common: more than 1 in 100 to less than 1 in 10). 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) in patients treated with nivolumab before or after transplant. 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 nivolumab in the past.

Also tell your healthcare professional before you are given Opdualag 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, 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 Opdualag 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 Opdualag after the expiry date which is stated on the carton and the vial label after EXP.

The expiry date refers to the last day of that month.

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

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

The unopened vials can be stored at controlled room temperature up to 25°C with room light for up to 72 hours.

Do not store any unused portion of the infusion solution for reuse. Any unused medicine or waste material should be disposed of in accordance with local requirements.

If you want more information about Opdualag:

- 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 calling 1-800-463-6267.

This leaflet was prepared by Bristol-Myers Squibb Canada

TMTrademark of Bristol-Myers Squibb Company used under licence by Bristol-Myers Squibb Canada

Last Revised SEP-2023