

OPDIVO®

(op-DEE-voh)

Nivolumab (nee-vol-u-mab)

Consumer Medicine Information

WARNINGS AND PRECAUTIONS - COMBINATION OF OPDIVO AND IPIILIMUMAB

Both OPDIVO and ipilimumab act on your immune system and may cause inflammation in parts of your body. Inflammation may cause serious damage to your body and some inflammatory conditions may be life-threatening.

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

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

WHAT IS IN THIS LEAFLET

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

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

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

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

WHAT IS OPDIVO USED FOR

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

Treatment with OPDIVO

OPDIVO is used to treat advanced skin cancer (unresectable or metastatic melanoma). OPDIVO is also used to treat skin cancer (melanoma) after surgical removal of the cancer.

OPDIVO is used to treat a type of lung cancer (advanced squamous and non squamous non-small cell lung cancer), a type of kidney cancer (clear cell renal cell carcinoma), a type of head and neck cancer (squamous cell cancer of the head and neck), a type of blood cancer called classical Hodgkin lymphoma, a type of bladder cancer (urothelial carcinoma) and a type of liver cancer (hepatocellular carcinoma) if your cancer has not responded, or if it has stopped responding, to earlier treatment.

Treatment with OPDIVO in combination with ipilimumab

OPDIVO in combination with ipilimumab is used to treat advanced melanoma in adults and a type of advanced kidney cancer (renal cell carcinoma).

Treatment with OPDIVO in combination with ipilimumab and chemotherapy

OPDIVO in combination with ipilimumab and chemotherapy is used to treat advanced lung cancer in adults.

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

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

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

Your doctor will continue giving you OPDIVO for as long as you keep benefitting from it or until you no longer tolerate the treatment.

Patients receiving OPDIVO after surgical removal of melanoma may require treatment for no longer than one year.

BEFORE YOU ARE GIVEN OPDIVO

You should not be given OPDIVO

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

Check with your doctor or nurse before you are given OPDIVO if:

- you have an autoimmune disease (a condition where the body attacks its own cells) like Crohn's, ulcerative colitis or lupus;
- you have any history of inflammation of the lungs
- you have been told your cancer has spread to your brain
- you have melanoma of the eye
- you were previously given ipilimumab, another medicine for the treatment of advanced melanoma, and experienced side effects because of this medicine.
- you are taking any medicines that suppress your immune system, such as corticosteroids, since these medicines may interfere with the effect of OPDIVO. However, once you are treated with OPDIVO, your doctor may give you corticosteroids to reduce any possible side effects that you may have during your treatment and this will not impact the effect of the medicine.

OPDIVO may cause:

- Problems with your lungs such as breathing difficulties, or cough. These may be signs of inflammation of the lungs (pneumonitis or interstitial lung disease).
- Diarrhoea (watery, loose or soft stools) or any symptoms of inflammation of the intestines (colitis), such as stomach pain and mucus or blood in the 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 decreased volume of urine, and kidney failure.
- Problems with your hormone producing glands (including the thyroid, parathyroid, pituitary, and adrenal glands) that may affect how these glands work. Signs and symptoms that your glands are not working properly may include fatigue (extreme tiredness), weight change or headache, muscle aches or cramps and visual disturbances.
- Diabetes (symptoms include excessive thirst, the passing of a greatly increased amount of urine, increase in appetite with a loss of weight, feeling tired, drowsy, weak, depressed, irritable and generally unwell) or diabetic ketoacidosis (acid in the blood produced from diabetes).
- Inflammation of the skin that can lead to rash and itching. Severe and possibly fatal peeling of the skin (toxic epidermal necrolysis, Steven-Johnson syndrome).
- Loss of the covering around the nerves (demyelination), inflammation of the nerves caused by the body attacking itself, causing numbness, weakness, tingling or burning pain.
- A condition in which the muscles become weak and tire easily (myasthenic syndrome).
- A temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain-Barré syndrome).
- Inflammation of the brain
- Inflammation of muscles causing pain or stiffness

- Inflammation of the heart (myocarditis) characterised by shortness of breath, fatigue, palpitations or chest pain
- Muscle breakdown/injury (rhabdomyolysis) characterised by muscle pain, weakness, nausea or vomiting.
- Solid organ transplant rejection.

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

Do not try to treat your symptoms with other medicines.

Complications of stem cell transplant that uses donor cells (allogeneic) may occur after treatment with Opdivo.

These complications can be severe and can lead to death. Your healthcare provider will monitor you for signs of complications if you have an allogeneic stem cell transplant.

Using other medicines

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

Children

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

Take special care with OPDIVO

OPDIVO is a medicine that influences your immune system and may cause inflammation in parts of your body. Inflammation can cause serious damage to your body and some inflammatory conditions may be life-threatening. Inflammation may cause serious damage to your body and some inflammatory conditions may be life threatening and need treatment or withdrawal of

OPDIVO. Tell your doctor immediately if you have any of the symptoms of inflammation listed in "Possible Side Effects".

Pregnancy and breast-feeding

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

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

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

- You must use effective contraception while you are being treated with OPDIVO if you are a woman who could become pregnant.
- If you become pregnant while using OPDIVO, tell your doctor.

You should stop breast-feeding if you are being treated with OPDIVO.

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

Driving and using machines

No studies on the effects on the ability to drive and use machines have been performed. OPDIVO is unlikely to affect your ability to drive or use machines; however, use caution when performing these activities until you are sure that OPDIVO does not adversely affect you.

Important information about some of the ingredients of OPDIVO

Tell your doctor if you are on a low-sodium (low-salt) diet before you are given OPDIVO. This medicine contains 2.5 mg sodium per mL of concentrate.

HOW OPDIVO IS GIVEN

OPDIVO will be given to you in hospital or clinic under the supervision of an experienced doctor.

It will be given to you as an infusion (a drip) into a vein (intravenously).

Your doctor will decide how many treatments you need.

Dosage and frequency of administration

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

Some types of cancer are treated with OPDIVO in combination with ipilimumab or ipilimumab and chemotherapy.

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

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 doctor.

If you miss a dose of OPDIVO

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

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 doctor.

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

WHILE YOU ARE BEING TREATED WITH OPDIVO

Things you must do

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

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

Please note that these signs and symptoms are sometimes delayed, and may develop weeks or months after your last dose. Before treatment, your doctor will check your general health. You will also have blood tests during treatment.

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

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

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

These symptoms may be:

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

POSSIBLE SIDE EFFECTS

Like all medicines, OPDIVO 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.

Do not try to treat your symptoms with other medicines.

Do not be alarmed by possible side effects.

You may not experience any of them.

Ask your doctor to answer any questions you may have.

The following side effects have been reported in clinical trials when OPDIVO has been given alone:

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

- Decrease in some white blood cells
- Diarrhoea (watery, loose or soft stools), nausea
- Skin rash sometimes with blisters, itching
- Feeling tired or weak

Common (may affect up to 1 in 10 people)

- Infections of the upper respiratory tract
- 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
- Inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs, headaches, dizziness
- Inflammation of the lungs (pneumonitis), characterised by coughing and difficulty breathing
- Coughing, shortness of breath (dyspnoea)
- Inflammation of the intestines (colitis)
- Stomach pain, constipation
- Mouth ulcers and cold sores (stomatitis), vomiting, dry mouth

- Skin colour changes in patches (vitiligo), dry skin, redness of the skin, hair loss or thinning
- Pain in the muscles, bones and joints
- Fever, oedema (swelling)
- Allergic reaction, reaction related to the infusion of the medicine
- High blood pressure (hypertension)

Uncommon (may affect up to 1 in 100 people)

- Serious lung infection (pneumonia), bronchitis
- Decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys), underactive function (hypopituitarism) or inflammation (hypophysitis) of the pituitary gland situated at the base of the brain, swelling of the thyroid gland, diabetes
- Inflammation of the pancreas, inflammation of the stomach (gastritis)
- Dehydration
- Increased acid level in the blood
- Increase in some white blood cells
- Inflammation of the eye, which causes pain and redness, blurred vision, dry eyes
- Inflammation in the kidney, kidney failure
- Fast heart rate
- Arthritis
- Damage to nerves causing numbness and weakness (polyneuropathy), inflammation of the nerves caused by the body attacking itself, causing numbness, weakness, tingling and burning pain
- Inflammation of the liver (hepatitis)
- Fluid around the lungs
- Severe condition of the skin that causes red, often itchy spots, similar to rash of measles, which starts on the limbs and sometimes

on the face and the rest of the body (erythema multiforme), skin disease with thickened patches of red skin, often silvery scales (psoriasis), skin conditions of the face where the nose and cheeks are unusually red (rosacea), hives (itchy, bumpy rash)

- Pain, chest pain

Rare (may affect up to 1 in 1000 people)

- Life threatening allergic reaction
- Severe and possibly fatal peeling of the skin (toxic epidermal necrolysis, Steven-Johnson syndrome)
- Loss of the covering around the nerves (demyelination) pain
- A condition in which the muscles become weak and tire easily (myasthenic syndrome)
- A temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain-Barré syndrome)
- Inflammation of the brain
- Ulcer of the small intestine
- Blockage of the bile ducts
- Fluid in lungs
- Acid in the blood produced from diabetes (diabetic ketoacidosis)
- A disease causing inflammation or enlargement of a lymph node (Kikuchi lymphadenitis)
- Changes in the rhythm or rate of the heart, abnormal heart rhythm
- Inflammation of the heart (myocarditis) characterised by shortness of breath, fatigue, palpitations or chest pain
- Inflammation of muscles causing pain or stiffness
- Muscle breakdown/injury (rhabdomyolysis) characterised by muscle pain, weakness, nausea or vomiting.
- Myopathy (aching muscles, muscle tenderness or weakness, not caused by exercise)
- Inflammatory disease of blood vessels

- Disease in which the immune system attacks the glands that make moisture for the body, such as tears and saliva (Sjogren's syndrome)
- decrease in parathyroid hormone
- blood disorder caused by overactive immune cells

Changes in test results

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

- Abnormal liver function tests
- Abnormal kidney function tests
- A decreased number of red blood cells (which carry oxygen), white blood cells (which are important in fighting infection) or platelets (cells which help the blood clot)
- Abnormal levels of calcium, potassium, magnesium or sodium in your blood
- Decrease in body weight
- Higher levels of sugar in your blood (hyperglycaemia)

The following side effects have been reported in clinical trials when OPDIVO has been given in combination with ipilimumab:

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

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

Common (may affect up to 1 in 10 people)

- Serious lung infection (pneumonia), infections of the upper respiratory tract
- Increase in some white blood cells
- Decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys); underactive function (hypopituitarism) or inflammation (hypophysitis) of the pituitary gland situated at the base of the brain; overactive thyroid gland, which can cause rapid heart rate, sweating and weight loss; inflammation of the thyroid gland (hyperthyroidism); swelling of the thyroid gland
- Dehydration
- Inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; dizziness
- Inflammation of the eye, which causes pain and redness, blurred vision
- Fast heart rate
- High blood pressure (hypertension)
- Inflammation of the lungs (pneumonitis), characterised by coughing and difficulty breathing, blood clots, cough
- Mouth ulcers and cold sores (stomatitis), inflammation of the pancreas (pancreatitis), constipation, dry mouth
- Inflammation of the liver
- Skin colour change in patches (vitiligo), dry skin, redness of the skin, unusual hair loss or thinning, hives (itchy rash)
- Pain in the muscles and bones
- Kidney failure (including abrupt loss of kidney function)
- Oedema (swelling), pain
- Allergic reaction, reactions related to the infusion of the medicine

Uncommon (may affect up to 1 in 100 people)

- Inflammation of the brain
- Bronchitis
- Chronic diseases associated with a build-up of inflammatory cells in various organs and tissues, most commonly the lungs (sarcoidosis)
- Acid in the blood produced from diabetes (diabetic ketoacidosis), diabetes
- A temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain-Barré syndrome); damage to nerves causing numbness and weakness (polyneuropathy); inflammation of the nerves; foot drop (peroneal nerve palsy); inflammation of the nerves caused by the body attacking itself, causing numbness, weakness, tingling or burning pain (autoimmune neuropathy)
- Changes in the rhythm or rate of the heart beat, abnormal heart rhythm
- Fluid around the lungs
- Intestinal perforation, inflammation of the stomach (gastritis), inflammation of the duodenum (duodenitis)
- Skin disease with thickened patches of red skin, often with silvery scales (psoriasis)
- Chronic disease of joints (spondyloarthritis)
- Disease in which the immune system attacks the glands that make moisture for the body, such as tears and saliva (Sjogren's syndrome)
- Inflammation of the joints (arthritis)
- Inflammation of muscles (myositis) causing pain or stiffness
- Inflammation of the kidney (nephritis)
- Chest pain

- Inflammation of the heart (myocarditis) characterised by shortness of breath, fatigue, palpitations or chest pain.
 - Muscle breakdown/injury (rhabdomyolysis) characterised by muscle pain, weakness, nausea or vomiting.
- Rare (may affect up to 1 in 1000 people)**
- Severe and possibly fatal peeling of the skin (toxic epidermal necrolysis, Steven-Johnson syndrome)
 - decrease in parathyroid hormone
 - blood disorder caused by overactive immune cells
- Changes in test results**
- OPDIVO in combination with ipilimumab may cause changes in the results of tests carried out by your doctor. These include:
- Abnormal liver function tests
 - Abnormal kidney function tests
 - A decreased number of red blood cells (which carry oxygen), white blood cells (which are important in fighting infection) or platelets (cells which help the blood to clot)
 - An increased level of the enzyme that breaks down fats and of the enzyme that breaks down starch.
 - Abnormal levels of calcium, potassium, magnesium or sodium in your blood
 - Higher blood levels of bilirubin
 - Decrease in body weight
 - Higher (hyperglycaemia) or lower (hypoglycaemia) levels of sugar in your blood
- The following side effects have been reported in clinical trials when OPDIVO has been given in combination with ipilimumab and chemotherapy:**
- Very common (may affect more than 1 in 10 people)**
- Underactive thyroid gland, which can cause tiredness or weight gain
 - Decreased appetite
 - diarrhoea (watery, loose or soft stools), vomiting, nausea
 - Skin rash sometimes with blisters, itching
 - Feeling tired or weak
 - **Common (may affect up to 1 in 10 people)**
 - Conjunctivitis
 - Serious lung infection (pneumonia), infections of the upper respiratory tract
 - Increase in some white blood cells
 - Allergic reaction, reactions related to the infusion of the medicine
 - Decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys), inflammation (hypophysitis) of the pituitary gland situated at the base of the brain, overactive thyroid gland, which can cause rapid heart rate, sweating and weight loss, swelling of the thyroid gland
 - Inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; dizziness
 - dry eyes
 - headache
 - Shortness of breath (dyspnoea)
 - Inflammation of the lungs (pneumonitis), characterised by coughing and difficulty breathing, blood clots, cough
 - Inflammation of the intestines (colitis)
 - Mouth ulcers and cold sores (stomatitis), inflammation of the pancreas (pancreatitis), constipation, dry mouth
 - Inflammation of the liver
 - dry skin, redness of the skin, unusual hair loss or thinning
 - Pain in the joints, muscles and bones, inflammation of the joints
 - Kidney failure (including abrupt loss of kidney function)
 - Fever
 - Oedema (swelling)
 - **Uncommon (may affect up to 1 in 100 people)**
 - underactive function (hypopituitarism) of the pituitary gland situated at the base of the brain, decrease in parathyroid hormone
 - damage to nerves causing numbness and weakness (polyneuropathy); inflammation of the nerves caused by the body attacking itself, causing numbness, weakness, tingling or burning pain (autoimmune neuropathy), inflammation of the brain
 - blurred vision
 - Changes in the rhythm or rate of the heart beat, abnormal heart rhythm
 - High blood pressure (hypertension), low blood pressure (hypotension)
 - Fluid around the lungs, bronchitis
 - Skin disease with thickened patches of red skin, often with silvery scales (psoriasis)
 - Severe and possibly fatal peeling of the skin (Steven-Johnson syndrome)
 - Inflammation of muscles (myositis) causing pain or stiffness
 - Inflammation of the kidney (nephritis)
 - Chest pain
- Changes in test results**
- OPDIVO in combination with ipilimumab and chemotherapy may cause changes in the results of tests carried out by your doctor. These include:
- Abnormal liver function tests
 - Abnormal kidney function tests
 - A decreased number of red blood cells (which carry oxygen), white blood cells (which are important in fighting infection) or platelets (cells which help the blood to clot)

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

FURTHER INFORMATION

What OPDIVO contains

- The active substance is nivolumab.

Each vial contains either 40 mg (in 4mL) or 100 mg (in 10mL) of nivolumab.

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

What OPDIVO looks like and contents of the pack

OPDIVO concentrate for solution for infusion is a clear to opalescent, colourless to pale yellow liquid that may contain light (few) particles.

It is available in packs containing either 1 vial of 40 mg in 4 mL or 1 vial of 100 mg in 10 mL.

HOW TO STORE OPDIVO

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.

Sponsored by

Bristol-Myers Squibb Australia Pty Ltd

4 Nexus Court, Mulgrave

Victoria 3170, Australia,

Registration Numbers:

OPDIVO (nivolumab) concentrate solution for infusion 40mg in 4mL (10mg/mL) AUST R 231867

OPDIVO (nivolumab) concentrate solution for infusion 100mg in 10mL (10mg/mL) AUST R 231868

OPDIVO (nivolumab) concentrate solution for infusion 240mg in 24mL (10mg/mL) AUST R 318057 (not marketed).

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