

OPDIVO®

(op-DEE-voh)

Nivolumab (nee-vol-u-mab)

Consumer Medicine Information

WARNINGS AND PRECAUTIONS - COMBINATION OF OPDIVO AND YERVOY IN THE TREATMENT OF ADVANCED MELANOMA

Both OPDIVO and Yervoy 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.

OPDIVO is used to treat advanced melanoma in adults.

OPDIVO in combination with YERVOY (ipilimumab) is used to treat advanced melanoma in adults.

OPDIVO is also used to treat advanced squamous and non squamous non-small cell lung cancer (a type of lung cancer) in adults. It is used if your cancer has not responded, or if it has stopped responding, to earlier treatment.

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

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 (YERVOY®), 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 gland (including the thyroid, 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 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 peeling of the skin.

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.

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. 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) over a period of 60 minutes, every 2 weeks. Your doctor will continue giving OPDIVO for as long as you keep benefitting from it or until you no longer tolerate the treatment.

OPDIVO is a concentrate solution for infusion. The amount of OPDIVO you will be given will be calculated based on your body weight.

Depending on your dose, some or all of the content of the OPDIVO vial may be diluted with saline or glucose solution before use. More than one vial may be necessary to obtain the required dose.

Dosage and frequency of administration

The recommended dose is 3 mg of OPDIVO per kilogram of your body weight for the treatment of metastatic melanoma and squamous and non squamous non small cell lung cancer.

If you have advanced melanoma your doctor may decide to give you

OPDIVO in combination with YERVOY.

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

When OPDIVO is given in combination with YERVOY the recommended dose of OPDIVO is 1mg of OPDIVO per kilogram of your body weight for the first 4 doses (combination phase). Thereafter the recommended dose of OPDIVO is 3mg of OPDIVO per kilogram of your body weight (single-agent phase).

Please refer to the package leaflet of YERVOY 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 adverse effects or if they get worse. See Possible Side Effects.

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

You 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.

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

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)

- Diarrhoea (watery, loose or soft stools), nausea
- Skin rash, itching
- Feeling tired or weak

Common (may affect up to 1 in 10 people)

- 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
- vision problems or blurry vision
- Inflammation of the lungs (pneumonitis), characterised by coughing, difficulty breathing; shortness of breath (dyspnoea)
- mouth ulcers and cold sores (stomatitis), vomiting, , stomach pain, constipation, dry mouth
- Skin colour changes in patches (vitiligo), dry 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

Uncommon (may affect up to 1 in 100 people)

- Inflammation of the thyroid gland
- Inflammation of the pancreas
- Dehydration
- Increase in some white blood cells
- Inflammation of the eye, which causes pain and redness,
- Inflammation in the kidney
- Bronchitis, Infections of the upper respiratory tract
- Adrenal glands not working properly, High sugar levels in the blood
- Fast heart rate
- Inflammation of the blood vessels
- Inflammation of muscles causing pain or stiffness
- Inflammation of the brain
- Inflammation of the intestines (colitis),
- inflammation of the nerves caused by the body attacking itself, causing numbness, weakness, tingling or burning pain
- Fluid around the lungs

Rare (may affect up to 1 in 1000 people)

- Severe and possibly fatal peeling of the skin (toxic epidermal necrolysis, Steven-Johnson syndrome)
- Loss of the covering around the nerves
- A temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain-Barré syndrome);
- gastritis (inflammation of the stomach)

Changes in test results

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

- Abnormal liver function tests (increased amounts of the liver enzyme aspartate aminotransferase, alanine

aminotransferase or alkaline phosphatase in your blood, higher blood levels or 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 clot)
- Abnormal levels of calcium, potassium, magnesium or sodium in your blood

The following side effects have been reported in clinical trials when OPDIVO has been given in combination with YERVOY:**Very common (may affect more than 1 in 10 people)**

- Underactive thyroid gland, which can cause tiredness or weight gain
- Decreased appetite
- Headache
- Inflammation of the intestines (colitis), diarrhoea (watery, loose or soft stools), vomiting, nausea, stomach pain
- Skin rash, itching
- Pain in the joints
- Feeling tired or weak, fever

Common (may affect up to 1 in 10 people)

- Infections of the upper respiratory tract, serious lung infection (pneumonia)
- 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; swelling of the thyroid gland, high sugar levels in the blood (hyperglycaemia)

- 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, vision problems or blurry vision
- Fast heart rate
- High blood pressure (hypertension)
- Inflammation of the lungs (pneumonitis), characterised by coughing and difficulty breathing, shortness of breath (dyspnoea)
- Mouth ulcers and cold sores (stomatitis), gastritis (inflammation of the stomach), 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
- 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
- Changes in the rhythm or rate of the heart beat, abnormal heart rhythm
- Fluid around the lungs
- Inflammation of the pancreas, intestinal perforation, inflammation of the duodenum
- Skin disease with thickened patches of red skin, often with silvery scales (psoriasis); severe and possibly fatal peeling of the skin (toxic epidermal necrolysis, Steven-Johnson syndrome)
- Chronic disease of joints (spondyloarthropathy)
- 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 kidney
- Chest pain

Changes in test results

OPDIVO in combination with YERVOY may cause changes in the results of tests carried out by your doctor. 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 the waste product 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.
- Abnormal levels of calcium, potassium, magnesium or sodium in your blood
- Higher blood levels of bilirubin
- Decrease in body weight

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.
Before dilution, each one mL of sterile concentrate contains 10 mg of nivolumab.
- The other ingredients are sodium citrate, 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.

Keep OPDIVO out of the reach and sight of children.

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

From a microbiological point of view, once opened, the medicinal product should be infused or diluted immediately.

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

Date of preparation:

8 April 2016

OPDIVO® (nivolumab) and YERVOY® (ipilimumab) are registered trademarks of Bristol-Myers Squibb Company