

MEDICATION GUIDE
OPDIVO® (op-DEE-voh)
(nivolumab)
injection

Read this Medication Guide before you start receiving OPDIVO and before each infusion. There may be new information. If your healthcare provider prescribes OPDIVO in combination with ipilimumab, also read the Medication Guide that comes with ipilimumab. If your healthcare provider prescribes OPDIVO in combination with cabozantinib, also read the Patient Information that comes with cabozantinib. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about OPDIVO?

OPDIVO is a medicine that may treat certain cancers by working with your immune system. OPDIVO can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended. You may have more than one of these problems at the same time. Some of these problems may happen more often when OPDIVO is used in combination with another therapy.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems.

- cough
- shortness of breath
- chest pain

Intestinal problems.

- diarrhea (loose stools) or more frequent bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdominal) pain or tenderness

Liver problems.

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than normal

Hormone gland problems.

- headaches that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems.

- decrease in your amount of urine
- blood in your urine
- swelling of your ankles
- loss of appetite

Skin problems.

- rash
- itching
- skin blistering or peeling
- swollen lymph nodes
- painful sore or ulcers in mouth or nose, throat, or genital area
- fever or flu-like symptoms

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with OPDIVO. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:

- chest pain, irregular heartbeat, shortness of breath or swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

Rejection of a transplanted organ or tissue. Your healthcare provider should tell you what signs and symptoms you should report and monitor you depending on the type of organ transplant that you have had.

Getting medical treatment right away may help keep these problems from becoming more serious. Your healthcare provider will check you for these problems during treatment with OPDIVO. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with OPDIVO, if you have severe side effects.

What is OPDIVO?

OPDIVO is a prescription medicine used to treat:

- **adults and children 12 years of age and older with a type of skin cancer called melanoma.**
 - OPDIVO may be used alone or in combination with ipilimumab to treat melanoma that has spread or cannot be removed by surgery (advanced melanoma), **or**
 - OPDIVO may be used alone to help prevent Stage IIB, Stage IIC, Stage III or Stage IV melanoma from coming back after it has been completely removed by surgery.
- **adults with a type of lung cancer called non-small cell lung cancer (NSCLC).**
 - OPDIVO may be used in combination with chemotherapy that contains platinum and another chemotherapy medicine before you have surgery for early-stage NSCLC,
 - OPDIVO may be used in combination with chemotherapy that contains platinum and another chemotherapy medicine before you have surgery for early-stage NSCLC:
 - that does not have an abnormal EGFR or ALK gene, **and**
 - then may be continued alone after surgery to help prevent your lung cancer from coming back.
 - OPDIVO may be used in combination with ipilimumab as your first treatment for NSCLC:
 - when your lung cancer has spread to other parts of your body (metastatic), **and**
 - your tumors are positive for PD-L1, but do not have an abnormal EGFR or ALK gene.
 - OPDIVO may be used in combination with ipilimumab and 2 cycles of chemotherapy that contains platinum and another chemotherapy medicine, as the first treatment of your NSCLC when your lung cancer:
 - has spread, or comes back, **and**
 - your tumor does not have an abnormal EGFR or ALK gene.
 - OPDIVO may be used when your lung cancer:
 - has spread, **and**
 - you have received chemotherapy that contains platinum, and it did not work or is no longer working, **and**
 - if your tumor has an abnormal EGFR or ALK gene, you should have also received an EGFR or ALK inhibitor medicine and it did not work or is no longer working.
- **adults with a type of cancer that affects the lining of the lungs and chest wall called malignant pleural mesothelioma.**
 - OPDIVO may be used in combination with ipilimumab as your first treatment for malignant pleural mesothelioma that cannot be removed by surgery.
- **adults with a type of kidney cancer called renal cell carcinoma (RCC).**
 - OPDIVO may be used in combination with ipilimumab as your first treatment for certain people when your cancer has spread (advanced RCC).
 - OPDIVO may be used in combination with cabozantinib as your first treatment when your cancer has spread (advanced RCC).
 - OPDIVO may be used alone when your cancer has spread after treatment with other cancer medicines.
- **adults with a type of blood cancer called classical Hodgkin lymphoma (cHL).**
 - OPDIVO may be used if:
 - 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 medicine brentuximab vedotin before or after your stem cell transplant, **or** you received at least 3 kinds of treatment including a stem cell transplant that uses your own stem cells (autologous).
- **adults with head and neck cancer (squamous cell carcinoma).**
 - OPDIVO may be used when your head and neck cancer:
 - has come back or spread, **and**
 - you have received chemotherapy that contains platinum and it did not work or is no longer working.
- **adults with a type of cancer of the lining of the urinary tract called urothelial carcinoma (UC).**
 - OPDIVO may be used 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 has spread or cannot be removed by surgery.

- OPDIVO may be used when your urinary tract cancer has spread (locally advanced or metastatic), **and**:
 - you have received chemotherapy that contains platinum, and it did not work or is no longer working, **or**
 - your cancer worsened within 12 months of treatment with chemotherapy that contains platinum, either before or after surgery to remove your cancer.
- **adults and children 12 years of age and older, with a type of colon or rectal cancer (colorectal cancer).**
 - OPDIVO may be used in combination with ipilimumab when your colon or rectal cancer:
 - cannot be removed with surgery, or has spread, **and**
 - is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).
 - OPDIVO may be used alone when your colon or rectal cancer:
 - has spread, **and**
 - is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), **and**
 - you have received treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, and it did not work or is no longer working.
- **adults with a type of liver cancer called hepatocellular carcinoma (HCC).**
 - OPDIVO may be used in combination with ipilimumab as your first treatment when your liver cancer:
 - cannot be removed by surgery, **or**
 - has spread.
 - OPDIVO may be used in combination with ipilimumab when your liver cancer:
 - cannot be removed by surgery, **or**
 - has spread, and
 - you have received prior treatment with sorafenib.
- **adults with cancer of the tube that connects your throat to your stomach (esophageal cancer).**
 - OPDIVO may be used to help prevent your esophageal or gastroesophageal junction cancer from coming back when:
 - your esophageal or gastroesophageal junction cancer has been treated with chemoradiation followed by surgery to completely remove the cancer, **but**
 - some cancer cells were still present in the removed tumor or lymph nodes.
 - OPDIVO may be used in combination with chemotherapy that contains fluoropyrimidine and platinum as your first treatment when your esophageal cancer:
 - is a type called squamous cell carcinoma, **and**
 - cannot be removed with surgery, or has spread, **and**
 - your tumors are positive for PD-L1.
 - OPDIVO may be used in combination with ipilimumab as your first treatment when your esophageal cancer:
 - is a type called squamous cell carcinoma, **and**
 - cannot be removed with surgery, or has spread, **and**
 - your tumors are positive for PD-L1.
 - OPDIVO may be used alone when your esophageal cancer:
 - is a type called squamous cell carcinoma, **and**
 - cannot be removed with surgery, and has come back or spread, **and**
 - you have received chemotherapy that contains fluoropyrimidine and platinum.
- **adults with cancer of the stomach (gastric cancer), cancer where the esophagus joins the stomach (gastroesophageal junction cancer), and in adults with esophageal adenocarcinoma.**
 - OPDIVO may be used in combination with chemotherapy that contains fluoropyrimidine and platinum when your gastric, gastroesophageal junction, or esophageal cancer:
 - cannot be removed with surgery, or has spread, **and**
 - your tumors are positive for PD-L1.

It is not known if OPDIVO is safe and effective in children younger than 12 years of age with melanoma or MSI-H or dMMR metastatic colorectal cancer.

It is not known if OPDIVO is safe and effective in children for the treatment of any other cancers.

Before receiving OPDIVO, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus.
- have received an organ transplant, including corneal transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area in the past and have received other medicines that are like OPDIVO
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. OPDIVO can harm your unborn baby.

Females who are able to become pregnant:

- Your healthcare provider should do a pregnancy test before you start receiving OPDIVO.
- You should use an effective method of birth control during treatment and for 5 months after your last dose of OPDIVO. Talk to your healthcare provider about birth control methods that you can use during this time.
- Tell your healthcare provider right away if you become pregnant during treatment with OPDIVO.
- are breastfeeding or plan to breastfeed. It is not known if OPDIVO passes into your breast milk. Do not breastfeed during treatment and for 5 months after your last dose of OPDIVO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive OPDIVO?

- Your healthcare provider will give you OPDIVO into your vein through an intravenous (IV) line over 30 minutes.
- When OPDIVO is used alone, it is usually given every 2 weeks or 4 weeks depending on the dose you are receiving.
- When OPDIVO is used in combination with ipilimumab (except for treating NSCLC), OPDIVO is usually given every 3 weeks, for up to 4 doses. Ipilimumab will be given on the same day. After that, OPDIVO will be given alone every 2 weeks or 4 weeks depending on the dose you are receiving.
- For NSCLC before you have surgery, OPDIVO is given in combination with platinum-containing chemotherapy and another chemotherapy medicine every 3 weeks for 3 cycles. In some cases, OPDIVO is used in combination with chemotherapy every 3 weeks for up to 4 cycles before you have surgery, followed by OPDIVO used alone every 4 weeks after you have surgery for up to 1 year.
- For NSCLC that has spread to other parts of your body, when OPDIVO is used in combination with ipilimumab, OPDIVO is given every 3 weeks, and ipilimumab is given every 6 weeks for up to 2 years. Your healthcare provider will determine if you will also need to receive chemotherapy every 3 weeks for 2 cycles.
- For malignant pleural mesothelioma, OPDIVO is given every 3 weeks and ipilimumab is given every 6 weeks for up to 2 years.
- For RCC, when used in combination with cabozantinib, OPDIVO is usually given every 2 weeks or 4 weeks depending on the dose you are receiving. Cabozantinib is given once daily by mouth.
- For UC that has spread to other parts of your body or cannot be removed by surgery, when OPDIVO is used in combination with chemotherapy medicines cisplatin and gemcitabine, OPDIVO is given every 3 weeks for up to 6 cycles. Chemotherapy will be given on the same day. After that, OPDIVO will be given alone every 2 weeks or 4 weeks depending on the dose you are receiving.
- When OPDIVO is used in combination with fluoropyrimidine- and platinum-containing chemotherapy for treating esophageal squamous cell carcinoma (ESCC), OPDIVO is given either every 2 weeks or every 4 weeks, for up to 2 years.
- When OPDIVO is used in combination with ipilimumab for esophageal squamous cell carcinoma, OPDIVO is given every 2 weeks or 3 weeks and ipilimumab is given every 6 weeks for up to 2 years.
- For gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma, when used in combination with fluoropyrimidine and platinum-containing chemotherapy, OPDIVO is given every 2 weeks or 3 weeks depending on the dose you are receiving, for up to 2 years. Chemotherapy will be given on the same day.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of OPDIVO?

OPDIVO can cause serious side effects, including:

- **See “What is the most important information I should know about OPDIVO?”**
- **Severe infusion reactions.** Tell your healthcare provider or nurse right away if you get these symptoms during an infusion of OPDIVO:

○ chills or shaking	○ dizziness
○ itching or rash	○ feel like passing out
○ flushing	○ fever
○ shortness of breath or wheezing	○ back or neck pain
- **Complications of stem cell transplant that uses donor stem cells (allogeneic).** These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with OPDIVO. Your healthcare provider will monitor you for signs of complications if you have an allogeneic stem cell transplant.

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

- | | |
|--------------------------------------|----------------------|
| ● feeling tired | ● constipation |
| ● rash | ● decreased appetite |
| ● pain in muscles, bones, and joints | ● back pain |

- itching
- diarrhea
- nausea
- weakness
- cough
- shortness of breath
- upper respiratory tract infection
- fever
- headache
- stomach-area (abdominal) pain
- vomiting
- urinary tract infection

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

- feeling tired
- diarrhea
- rash
- itching
- nausea
- pain in muscles, bones, and joints
- fever
- cough
- decreased appetite
- vomiting
- stomach-area (abdominal) pain
- shortness of breath
- upper respiratory tract infection
- headache
- low thyroid hormone levels (hypothyroidism)
- constipation
- decreased weight
- dizziness

The most common side effects of OPDIVO when used in combination with a platinum-containing chemotherapy and another chemotherapy medicine include:

- nausea
- feeling tired
- pain in muscles, bones and joints
- constipation
- decreased appetite
- rash
- vomiting
- numbness, pain, tingling, or burning in your hands and feet

The most common side effects of OPDIVO when used in combination with ipilimumab, a platinum-containing chemotherapy, and another chemotherapy medicine include:

- feeling tired
- pain in muscles, bones, and joints
- nausea
- diarrhea
- rash
- decreased appetite
- constipation
- itching

The most common side effects of OPDIVO when used in combination with cabozantinib include:

- diarrhea
- feeling tired or weak
- liver problems. See **“What is the most important information I should know about OPDIVO?”**
- rash, redness, pain, swelling or blisters on the palms of your hands or soles of your feet
- mouth sores
- rash
- high blood pressure
- low thyroid hormone levels
- pain in muscles, bones, and joints
- decreased appetite
- nausea
- change in the sense of taste
- stomach-area (abdominal) pain
- cough
- upper respiratory tract infection

The most common side effects of OPDIVO when used in combination with fluoropyrimidine and platinum-containing chemotherapy include:

- nausea
- numbness, pain, tingling, or burning in your hands or feet
- decreased appetite
- feeling tired
- constipation
- mouth sores
- diarrhea
- vomiting
- stomach-area (abdominal) pain
- pain in muscles, bones, and joints

These are not all the possible side effects of OPDIVO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of OPDIVO.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about OPDIVO that is written for health professionals.

What are the ingredients in OPDIVO?

Active ingredient: nivolumab

Inactive ingredients: mannitol, pentetic acid, polysorbate 80, sodium chloride, sodium citrate dihydrate, and Water for Injection. May contain hydrochloric acid and/or sodium hydroxide.

Manufactured by: Bristol-Myers Squibb Company, Princeton, NJ 08543 USA U.S. License No. 1713

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For more information, call 1-855-673-4861 or go to www.OPDIVO.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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