

Patient Pocket Guide

A guide to identify signs and symptoms of potential side effects while on immunotherapy, including immune-mediated side effects

1 Detach the wallet card and keep on your person at all times

- Fill out the treating oncologist's contact information

2 Read the information inside and use the Signs and Symptoms Checklist to recognize what to report immediately

- Call your oncologist right away if you experience anything unusual while on OPDIVO® or YERVOY®
- Contact your oncologist immediately if you experience any symptoms listed on this Signs and Symptoms Checklist, or they get worse.

Getting medical treatment right away may help prevent these problems from becoming more serious

3 Show this wallet card during any visits outside of healthcare network

- Tell the urgent care/emergency room staff that you are being treated with OPDIVO® or YERVOY®, and show them the important information for Doctors'/Nurses' section of this wallet card

Please check the box to indicate which immunotherapy the patient is receiving

OPDIVO®

OPDIVO® + YERVOY®

YERVOY®

To obtain a copy of this pocket guide please contact Bristol Myers Squibb by phone: 03-5231021 or fax: 03-9226896

Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8-13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®

Detach the wallet card and keep on your person at all times

- Fill out name of immunotherapy drug(s) prescribed by oncologist
- Fill out patient name
- Fill out name and phone number of oncologist
- Keep card in patient's wallet

Be sure to tell all healthcare providers you visit that you are being treated with immunotherapy **and SHOW THEM THIS CARD.**

Show this wallet card during any urgent care/emergency room visit

גא להתקשר לאונקולוג שלי. Please call my oncologist.
I have received an immunotherapy called: **קיבלתי טיפול אימונותרפי הנקרא:**

שם התכשיר(ים): **OPDIVO®/YERVOY®/OPDIVO® + YERVOY®**
(סמן את המנחים)

שם המטופל/ת:

שם האונקולוג:

מספר טלפון של האונקולוג:

Present this card **every time** you visit a healthcare provider

©2023 Bristol-Myers Squibb Company. All rights reserved.

כרטיס זה אושר בהתאם להוראות משרד הבריאות בינואר 2023

חשוב מידע עבור רופאים/אחיות

הגישה לטיפול בתופעות לוואי הנגרמות מאימונותרפיה עשויה להיות שונה מטיפולים אחרים לסרטן
אין להמתין עם הענקת טיפול למטופל במקרה שנדרש טיפול דחוף



למידע נוסף יש לעיין בעלון לרופא הישראלי של אופדיבו ושל יירבו.
ניתן לדווח על תופעות לוואי למשרד הבריאות באמצעות הטופס המקוון לדיווח על תופעות לוואי שבמצא בדף הבית של אתר משרד הבריאות: www.health.gov.il או על ידי כניסה לקישור: <https://sideeffects.health.gov.il>



Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8-13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®

Keep this guide handy for your reference. This guide includes a helpful checklist of Signs and Symptoms for you to closely monitor.

Call your Oncology Care Team if you have any of these signs or symptoms, or if they get worse.

These are not all of the possible side effects of OPDIVO® (nivolumab) or YERVOY® (ipilimumab). This is why you need to report any discomfort or changes in the way you are feeling to your Oncology Care Team.

Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8-13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®



Liver

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



Other Organs

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

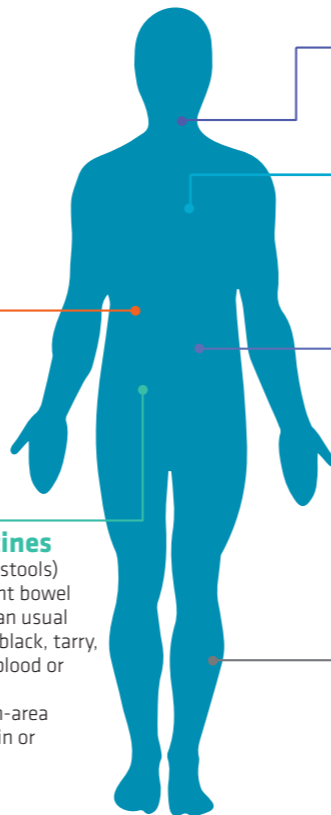
- Chest pain, irregular heartbeat, shortness of breath, or swelling of ankles
- Confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- Double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- Persistent or severe muscle pain or weakness, muscle cramps
- Low red blood cells count, predisposition to bruising

YERVOY® may be associated with eye problems with signs and symptoms that include blurry vision, double vision or other vision problems and eye pain or redness



Intestines

- 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



Lungs

- new or worsening cough
- shortness of breath
- chest pain



Kidneys

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



Hormone Glands

- 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 thirsty or hungry than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- voice changes, getting deeper and lower
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness



Skin

- rash
- itching
- skin blistering or skin peeling
- painful sores or ulcers in mouth or nose, throat, or genital area



Severe Infusion-Related Side effects

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feeling like passing out
- fever
- back or neck pain

Do not treat symptoms yourself

Symptoms may occur anytime during treatment or even after your treatment has ended

Do not feel embarrassed or that you are bothering your oncologist

Complications, including graft-versus-host disease (GVHD), in patients who have undergone bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications may be severe and may lead to death. These complications may happen if you underwent transplantation either before or after being treated with OPDIVO® or YERVOY®. Your healthcare provider will monitor you for signs of complications.

Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8-13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®

Important Safety Information

OPDIVO® (nivolumab) and YERVOY® (ipilimumab) are medicines that may treat certain types of cancer by activating your immune system. OPDIVO® and YERVOY® may cause your immune system to attack healthy tissues and organs in any area of your body and can affect the way they work. These problems may sometimes become serious or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended. You may experience 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 YERVOY® or another therapy.

YERVOY® can cause serious side effects in many parts of your body which can lead to death. These problems may happen anytime during treatment with YERVOY® or after you have completed treatment.

IMPORTANT Reminders for Patients

- Contact your oncologist immediately if you experience any symptoms listed on this Signs and Symptoms Checklist or if they get worse, or if you experience anything unusual while on OPDIVO® (nivolumab) or YERVOY® (ipilimumab) therapy. Getting medical treatment right away may help prevent these problems from becoming more serious
- These are not all of the possible side effects of OPDIVO® or YERVOY®. This is why you need to report any discomfort or changes in the way you are feeling to your Oncology Care Team
- Do not treat Signs and Symptoms yourself without talking to your oncologist
- Your oncologist may decide to delay or completely stop OPDIVO®, OPDIVO® + YERVOY® or YERVOY®, or give you other medicines to treat your symptoms

Important Safety Information for OPDIVO® (nivolumab), YERVOY® (ipilimumab), and OPDIVO® (nivolumab) + YERVOY® (ipilimumab)

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

OPDIVO® and YERVOY® are medicines that may treat certain types of cancer by activating your immune system. OPDIVO® and YERVOY® may cause your immune system to attack healthy tissues and organs in any area of your body and can affect the way they work. These problems may sometimes become serious or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended. You may experience 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 YERVOY® or another therapy.

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

- **Lung problems:** new or worsening 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 the 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 thirsty or hungry than usual; urinating more often than usual; hair loss; feeling cold; constipation; voice changes, getting deeper and lower; 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 in your ankles; loss of appetite
- **Skin problems:** rash; itching; skin blistering or skin peeling; painful sores or ulcers in the mouth or nose, throat, or genital area
- **Eye problems:** blurry vision, double vision, or other vision problems; eye pain or redness.

Important Safety Information for OPDIVO® (nivolumab), YERVOY® (ipilimumab), and OPDIVO® (nivolumab) + YERVOY® (ipilimumab)(continued)

Problems may also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that may happen with OPDIVO® and YERVOY®. 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 count, predisposition to bruising

Getting medical help right away may help prevent these problems from becoming more serious. Your doctor will check you for these problems during treatment and may treat you with corticosteroid or hormone replacement medicines. Your doctor may also need to delay or

completely stop your treatment if you have severe side effects.

Possible side effects of OPDIVO® and YERVOY® OPDIVO® and YERVOY® can cause serious side effects, including:

- **See “What is the most important information I should know about OPDIVO® and YERVOY®?”**
- **Severe infusion-related side effects.** Tell your healthcare team right away if you get these symptoms during an infusion of OPDIVO® or YERVOY®: chills or shaking; itching or rash; flushing; shortness of breath or wheezing; dizziness; feeling like passing out; fever; back or neck pain
- **Complications, including graft-versus-host disease (GVHD), in patients who have undergone bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications may be severe and may lead to death. These complications may happen if you underwent transplantation either before or after being treated with OPDIVO® or YERVOY®. Your healthcare provider will monitor you for signs of complications.

Important Safety Information for OPDIVO® (nivolumab), YERVOY® (ipilimumab), and OPDIVO® (nivolumab) + YERVOY® (ipilimumab)(continued)

Very common side effects of OPDIVO®, when used alone, include: feeling tired; weakness, generally feeling unwell; fever; swelling (edema), including swelling of the hands, ankles or feet (peripheral edema); diarrhea; nausea; vomiting; stomach-area (abdominal) pain; constipation; swollen stomach; dyspepsia; difficulty swallowing; rash; itchy skin including widespread itching; vitiligo [a disease in which light patches appear on the skin]; erythema [a disease manifested by skin redness and inflammation]; pain in muscles, bones, and joints; headache; dizziness; upper respiratory tract infection; nasal congestion; pneumonia, including pneumonia involving the bronchi; cough, cough with phlegm; shortness of breath, shortness of breath upon exertion; decreased appetite; decreased weight; back pain; low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid gland)] that can cause fatigue and weight gain; high thyroid hormone levels [hyperthyroidism (increased activity of the thyroid gland)] that can cause rapid heart rate, sweating and weight loss; thyroid gland problems, including thyroid gland inflammation (thyroiditis); abnormal renal function; urinary tract infection; liver inflammation (hepatitis); high blood pressure; high level of sugar in

blood (hyperglycemia); difficulty sleeping; numbness, pain, tingling or burning in the hands or feet (peripheral neuropathy); abnormal laboratory test results; infusion-related reactions.

Very common side effects of OPDIVO®, when used in combination with chemotherapy, include: feeling tired; generally feeling unwell; nausea; constipation; vomiting; decreased appetite; rash; hair loss; numbness, pain, tingling or burning in the hands or feet (peripheral neuropathy); abnormal laboratory test results.

Very common side effects of OPDIVO®, when used in combination with YERVOY®, include: feeling tired; fever; swelling (edema); rash; itching; widespread itching; dry skin; diarrhea; nausea; vomiting; stomach-area (abdominal) pain; constipation; swollen stomach (abdomen) due to fluid accumulation (ascites); dry mouth; dyspepsia; difficulty swallowing; ulcers or sores in the mouth (stomatitis); inflammation of the colon (colitis); pain in muscles, bones, and joints; cough, cough with phlegm; shortness of breath, shortness of breath upon exertion; pneumonia; upper respiratory tract infection; inflammation of the lung tissues (pneumonitis)

Important Safety Information for OPDIVO® (nivolumab), YERVOY® (ipilimumab), and OPDIVO® (nivolumab) + YERVOY® (ipilimumab)(continued)

characterized by coughing and difficulty breathing, shortness of breath and cough; decreased appetite; headache; dizziness; flu; flu-like illness; weakness, generally feeling unwell; chills; low blood pressure; low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid gland)] that can cause fatigue and weight gain; high thyroid hormone levels [hyperthyroidism (increased activity of the thyroid gland)] that can cause rapid heart rate, sweating and weight loss; adrenal glands insufficiency (decrease in the level of hormones secreted by adrenal glands located above the kidneys); decreased weight; difficulty sleeping; abnormal laboratory test results.

Very common side effects of OPDIVO®, when used in combination with YERVOY® and chemotherapy, include: feeling tired; fever; pain in muscles, bones, and joints; nausea; diarrhea; constipation; vomiting; stomach-area (abdominal) pain; rash; itching, including widespread itching; hair loss; decreased appetite; cough; shortness of breath; low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid gland)] that can cause fatigue and weight gain; headache; dizziness; abnormal laboratory test results.

Very common side effects of OPDIVO®, when used in combination with cabozantinib, include: diarrhea; nausea; stomach-area (abdominal) pain; vomiting; dyspepsia; feeling tired or weak; liver problems; liver toxicity; rash, redness, pain, swelling or blisters on the palms of your hands or soles of your feet; sores or ulcers in the mouth (stomatitis); rash; itching; high blood pressure; low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid gland)] that can cause fatigue and weight gain; pain in muscles, bones, and joints; decreased appetite; change in the sense of taste; headache; cough; voice disorders (difficulty speaking due to disorders of the pharynx, vocal cords, tongue or mouth); upper respiratory tract infection; abnormal laboratory test results.

Very common side effects of OPDIVO® when used in combination with fluoropyrimidine and platinum-containing chemotherapy include: numbness, pain, tingling, or burning in the hands or feet (peripheral neuropathy); headache; nausea; diarrhea; vomiting; difficulty swallowing; stomach-area (abdominal) pain; constipation; ulcers or sores in the mouth (stomatitis); feeling tired; fever; swelling (edema); decreased appetite; decreased weight; pain in muscles, bones, and joints; rash; itching; hair loss; rash, redness, pain, swelling or blistering

Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8–13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®

Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8–13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®

Important Safety Information for OPDIVO® (nivolumab), YERVOY® (ipilimumab), and OPDIVO® (nivolumab) + YERVOY® (ipilimumab)(continued)

of the hands or feet; cough, cough with phlegm; upper respiratory tract infection; pneumonia; difficulty sleeping; abnormal laboratory test results.

Very common side effects of YERVOY® include: feeling tired; diarrhea; nausea; itching; rash; vomiting; fever; decreased appetite; pain in muscles, bones, and joints; cough, cough with phlegm; shortness of breath, shortness of breath upon exertion; upper respiratory tract infection.

These are not all the possible side effects. For more information, ask your healthcare provider or pharmacist. You are encouraged to report side effects of prescription drugs to the Ministry of Health.

Side effects can be reported to the Ministry of Health by clicking on the "Reporting side effects following drug treatment" link found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or through the following link: <https://sideeffects.health.gov.il>

Important Safety Information for OPDIVO® (nivolumab), YERVOY® (ipilimumab), and OPDIVO® (nivolumab) + YERVOY® (ipilimumab)(continued)

Before treatment with OPDIVO® or YERVOY®, tell your healthcare provider about all of your medical conditions, including if:

- you have problems involving the immune system such as Crohn's disease, ulcerative colitis, or lupus
- you have received an organ transplant
- you have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- you have received radiation treatment to your chest area in the past and have received other medicines that are like OPDIVO®
- you have a condition that affects your nervous system, such as severe muscle weakness (myasthenia gravis) or Guillain-Barré syndrome
- you are pregnant or plan to become pregnant. OPDIVO® and YERVOY® may harm your unborn baby
- you are breastfeeding or plan to breastfeed. It is not known whether OPDIVO® or YERVOY® passes into your breast milk. Do not breastfeed during treatment with OPDIVO® and for 5 months after the last dose of OPDIVO®. Do not breastfeed during treatment with YERVOY® and for 3 months after the last dose of YERVOY®.

Females who are able to become pregnant:

Your healthcare provider should perform a pregnancy test before you start receiving OPDIVO® or YERVOY®.

- You should use an effective method of birth control during your treatment with OPDIVO® and for at least 5 months after receiving the last dose of OPDIVO®. You should use an effective method of birth control during your treatment with YERVOY® and for at least 3 months after receiving the last dose of YERVOY®.
- Consult your healthcare provider about birth control methods that you can use during this time. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with OPDIVO® or YERVOY®

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

Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8-13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®

Please see Important Safety Information for OPDIVO® and YERVOY® on pages 8-13, and the Israeli Full Prescribing Information and Patient leaflet for OPDIVO® and YERVOY®

Your Signs and Symptoms Checklist

Do you have any signs or symptoms?

1. If you notice any discomfort or changes in the way you are feeling, contact your Oncology Care Team immediately.
 2. Getting medical treatment right away may help prevent these problems from becoming more serious. Do not try to treat possible side effects yourself.
 3. Your oncologist may decide to delay or completely stop OPDIVO® (nivolumab) or YERVOY® (ipilimumab), or give you other medicines to treat your symptoms.
- ▶ **These are not all of the possible side effects of OPDIVO® or YERVOY®. This is why you need to report any discomfort or changes in the way you are feeling to your Oncology Care Team. Signs or changes to look out for include:**



Liver

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



Lungs

- new or worsening cough
- shortness of breath
- chest pain



Kidneys

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



Hormone Glands

- 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 thirsty or hungry than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- voice changes, getting deeper and lower
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness



Other Organs

- Problems may also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that may happen with OPDIVO® or YERVOY®. 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 count, predisposition to bruising



Intestines

- 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



Skin

- rash
- itching
- skin blistering or skin peeling
- painful sores or ulcers in mouth or nose, throat, or genital area



Severe Infusion-Related Side effects

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feeling like passing out
- fever
- back or neck pain

YERVOY® may be associated with eye problems with signs and symptoms that include blurry vision, double vision, or other vision problems and eye pain or redness..

Complications, including graft-versus-host disease (GVHD), in patients who have undergone bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications may be severe and may lead to death. These complications may happen if you underwent transplantation either before or after being treated with OPDIVO® or YERVOY®. Your healthcare provider will monitor you for signs of complications.

If you experience a severe side effect, you may need to go to a *hospital emergency department*. If this happens, you need to:



- Bring the wallet card and a full list of your medications, including prescription medicines and over-the-counter medicines, vitamins, nutritional supplements and herbal supplements
- Tell doctors and nurses in the emergency department that **you are on an immunotherapy treatment** to treat your condition
- Make sure your Oncology Care Team is notified