PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

Concentrate for solution for intravenous infusion

The active ingredient and its concentration: For the list of inactive ingredients and allergens, please see section 2 under

Important information about some of this medicine's ingredients' and section 6 2. BEFORE USING THE MEDICINE: 'Further information'. Read this leaflet carefully in its entirety before using the medicine. This

questions, refer to the doctor or pharmacist. carefully read the patient leaflet that comes with ipilimumab as well. If the treating Before treatment with OPDIVO, tell the doctor about all of your medical doctor prescribes you OPDIVO in combined treatment with cabozantinib, carefully conditions, including if: ead the patient leaflet that comes with cabozantinib as well.

leaflet contains concise information about the medicine. If you have further

This leaflet does not take the place of talking with your treating doctor about your

Pocket guide and patient safety information card In addition to the leaflet, pocket guide and patient safety information card

The pocket guide and the card contain important safety information which you have to know before and during the treatment with OPDIVO, and which you must follow. Review the pocket guide, the card and the patient leaflet before you start using the medicine. Keep the card and the pocket guide for further review if required.

1. WHAT IS THIS MEDICINE INTENDED FOR? OPDIVO is used to treat:

are available for OPDIVO.

 A type of skin cancer called melanoma OPDIVO used alone or in combination with ipilimumab is indicated for Tests and follow up:

treatment of adults with advanced (unresectable or metastatic) melanoma. The treating doctor will perform blood tests to monitor side effects OPDIVO is indicated as complementary (adjuvant) treatment for patients with melanoma involving the lymph nodes or metastatic melanoma after complete

 Non-small cell lung cancer OPDIVO, in combination with platinum-doublet chemotherapy, is indicated as treatment before surgery (neoadjuvant) of adult patients with resectable

Pregnancy and breastfeeding (tumors ≥ 4 cm or involve lymph nodes) non-small cell lung cancer.

indicated as first-line treatment for adult patients with metastatic or recurrent OPDIVO is indicated for treatment of patients with metastatic non-small about birth control methods that you can use during this time.

treatment with platinum-based chemotherapy.

• Malignant pleural mesothelioma, cancer of mesothelial cells comprising

Do not breastfeed during treatment with OPDIVO and for 5 months after taking eye sensitivity to light adults with unresectable malignant pleural mesothelioma.

 Advanced renal cell carcinoma OPDIVO in combination with ipilimumab is indicated as first-line treatment for patients with advanced renal cell carcinoma at moderate or high risk. OPDIVO in combination with cabozantinib is indicated as first-line treatment

for patients with advanced renal cell carcinoma. OPDIVO used alone is indicated for the treatment of patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy. Classical Hodgkin lymphoma (a type of blood cancer)

that has come back or spread after: a stem cell transplant that uses your own stem cells (autologous), and treatment with brentuximab vedotin medicine or

 3 or more systemic treatment lines including a stem cell transplant that uses Squamous cell head and neck cancer (squamous cell carcinoma)

squamous cell head and neck cancer whose disease has progressed during or for an adult. following platinum-based chemotherapy.

Urothelial carcinoma (urinary tract or bladder cancer) OPDIVO is indicated as complementary (adjuvant) treatment for patients with Always use the medicine according to the doctor's instructions. urinary tract or bladder cancer at high risk of disease recurrence after radical

Check with your doctor or pharmacist if you are not sure about the dose or

• itching

OPDIVO is indicated for treatment of patients with locally advanced or

o after their disease has progressed during or following platinum-based

chemotherapy given prior to tumor resection surgery (neoadjuvant) or as Metastatic colon or rectal cancer (colorectal cancer)

metastatic colorectal cancer expressing dMMR (mismatch repair deficient) or SI-H (microsatellite instability-high), whose disease has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan. Liver cancer (hepatocellular carcinoma)

OPDIVO used alone or in combination with initimumab is indicated for patients Esophageal cancer

OPDIVO is indicated for the complementary (adjuvant) treatment after complete resection of esophageal cancer or gastroesophageal junction cancer with

carcinoma with PD-L1 expression in ≥ 1% of the tumor cells.

OPDIVO is indicated for treatment of patients with unresectable, advanced,

• When OPDIVO is used in combination with ipilimumab for treating esophageal

OPDIVO in combination with fluoropyrimidine and platinum containing chemotherapy is indicated for treatment of patients with unresectable, advanced or metastatic gastric cancer, gastroesophageal junction cancer or esophageal

Therapeutic group: antineoplastic agent

• you are sensitive (allergic) to the active ingredient (nivolumab) or to any of Adhere to the treatment regimen as recommended by the doctor.

the other ingredients in this medicine (see section 6).

Special warnings regarding use of this medicine • you have problems involving the immune system such as Crohn's disease,

pass it on to others. It may harm them, even if it seems to you that their ailment

• you have had an organ transplar you have received or are about to receive a stem cell transplant that uses donor stem cells (allogeneic)

> received other medicines that are like OPDIVO you have a condition that affects your nervous system, such as severe muscle OPDIVO may cause serious side effects, including: weakness (myasthenia gravis) or Guillain-Barré syndrome

breastfeeding') Children and adolescents

There is no information regarding the efficacy and safety of OPDIVO:

in children below the age of 12 with metastatic colorectal cancer expressing dMMR or MSI-H, or in children below the age of 18 for the treatment of other cancer types

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor of

DPDIVO, in combination with ipilimumab and 2 treatment cycles of combined Women who are able to become pregnant:

salt) per each ml of the concentrated solution.

The treating doctor should perform a pregnancy test before you start receiving Liver problems. platinum-containing chemotherapy (platinum-doublet chemotherapy) is • You should use an effective method of birth control during treatment and for • severe nausea or vomiting 5 months after receiving the last dose of OPDIVO. Consult your treating doctor • pain on the right side of the stomach area (abdomen) cell lung cancer whose disease has progressed during treatment or after

• Tell the treating doctor right away if you become pregnant during treatment

• bleeding or bruising more easily than normal

D in combination with pilimumab is indicated as first-line treatment for the last dose of OPDIVO. It is not known whether OPDIVO can pass into your

Driving and operating machinery Exercise caution when driving or using any tools or machines until you are certain extreme tiredness that OPDIVO does not adversely affect you as a result of potential side effects • weight gain or weight loss (see section 4) Children should be warned against riding bicycles or playing near the road, etc.

• urinating more often than usual

Important information about some of this medicine's ingredients OPDIVO contains sodium. you consume a low sodium (low salt) diet, inform your doctor prior to administration • constipati f this medicine. The medicine contains 2.5 mg sodium (the major ingredient of cooking salt/table dizziness or fainting

The medicine contains 10 mg sodium in each 4 ml vial. This quantity is equivalent to 0.5% of the recommended maximal daily dietary intake of sodium for an adult. Kidney problems. The medicine contains 25 mg sodium in each 10 ml vial. This quantity is blood in your urine OPDIVO is indicated for treatment of patients with recurrent or metastatic equivalent to 1.5% of the recommended maximal daily dietary intake of sodium

3. HOW SHOULD YOU USE THE MEDICINE?

about how to take this medicine. The dosage and treatment regimen will be determined only by the doctor.

• painful sores or ulcers in mouth or nose, throat, or genital area OPDIVO is administered by healthcare professionals directly into the vein through an intravenous (IV) line over 60 minutes or 30 minutes, depending on all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs and symptoms of immune system problems that may all of the signs are signs and symptoms of immune system problems that may all of the signs are signs and symptoms of immune system problems that may all of the signs are signs and symptoms of immune system problems that may all of the signs are signs are signs are signs and symptoms of immune system problems that may all of the signs are sig • When OPDIVO is used alone, it is usually given every 2 weeks or every 4 weeks

depending on the dose you are receiving. When OPDIVO is used in combination with ipilimumab, except for treating
 chest pain, irregular heartbeat, shortness of breath or swelling of ankles metastatic non-small cell lung cancer and for treating some cases of malignant OPDIVO used alone or in combination with ipilimumab is indicated for treatment of adult and pediatric patients aged 12 years and older with metastic colorated concerns at MAND (Combined to the control of the arms or legs and older with metastic colorated concerns at MAND (Combined to the control of the arms or legs and older with metastic colorated concerns at MAND (Combined to the arms or legs and older with a total of 4 treatment doses. Ipilimumab will be given on the same day. After the colorated concerns at MAND (Combined to the arms or legs are the arms or legs and the arms or legs are the arms or legs and the arms or legs are a total of 4 treatment doses. Iplimumab will be given on the same day. After that, OPDIVO will be given alone every 2 weeks or every 4 weeks depending on the dose you are receiving.

• severe or persistent muscle pain or weakness, muscle cramps on the dose you are receiving. on the dose you are receiving.

> OPDIVO is used in combination with chemotherapy every 3 weeks for 3 treatment from becoming more serious. OPDIVO is given every 3 weeks, and ipilimumab is given every 6 weeks for treatment with OPDIVO. up to 2 years. You will also need to receive chemotherapy every 3 weeks for
>
> Severe infusion-related side effects

2 treatment cycles. residual pathological disease in patients treated with chemoradiotherapy

• For treatment of malignant pleural mesothelioma, OPDIVO is given every 2 symptoms listed below when receiving the OPDIVO infusion: weeks or every 3 weeks and ipilimumab is given every 6 weeks for up to 2

• chills or shaking OPDIVO, in combination with fluoropyrimidine and platinum-based combination chemotherapy, is indicated for the first-line treatment of adult patients with unresectable, advanced, recurrent or metastatic esophageal squamous cell combination with cabozantinib, OPDIVO is usually given every 2 weeks or combination with cabozantinib, OPDIVO is usually given every 2 weeks or every 4 weeks depending on the dose you are receiving. Cabozantinib is given every 4 weeks depending on the dose you are receiving.

every 4 weeks depending on the dose you are receiving. Cabozantinib is given

• dizziness OPDIVO, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable, advanced, recurrent or when OPDIVO is used in combination with fluoropyrimidine and platinum-based • feel like • feer metastatic esophageal squamous cell carcinoma with PD-L1 expression in chemotherapy for treating esophageal squamous cell carcinoma, OPDIVO is back or neck pain

given every 2 weeks or every 4 weeks for up to 2 years.

treatment with fluoropyrimidine and platinum-based chemotherapy.

• Gastric cancer, gastroesophageal junction cancer and esophageal

• Fortreatment of gastric cancer, gastroesophageal junction cancer and esophageal

• Fortreatment of gastric cancer, gastroesophageal junctions may be severe and may lead to death. These complications

• rash

• rash

• these complications may be severe and may lead to death. These complications 3 weeks depending on the dose you are receiving for up to 2 years. Chemotherapy you have undergone an allogeneic stem cell transplant. will be given on the same day. The treating doctor will decide how many treatments you need. If you are unable to come in for your scheduled treatment, or if you forget to come.

in for treatment, contact the treating doctor as soon as possible to schedule a

• feeling tired new appointment for treatment. Do not exceed the recommended dose.

If you have taken an overdose, or if a child has accidentally swallowed • diarrhea some medicine, refer immediately to a doctor or proceed to a hospital nausea emergency room and bring the package of the medicine with you. Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist. 4. SIDE EFFECTS

Severe side effects related to immune system activity • you are pregnant or plan to become pregnant (see the section 'Pregnancy and OPDIVO is a medicine that treats certain types of cancer by activating your immune system. OPDIVO may cause your immune system to attack healthy • you are breastfeeding or plan to breastfeed (see the section 'Pregnancy and tissues and organs in any area of your body and can affect the way they work. These problems may sometimes become serious or lead to death. These problems may appear at any time during treatment or even after 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 ombination with additional treatment

Immediately contact the treating doctor if you experience any new signs or symptoms or worsening signs or symptoms, including: Lung problems.

 onset of cough or worsening cough 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 rellowing of your skin or the whites of your eyes

 dark urine (tea colored) Hormone glands problems.

headaches that will not go away or unusual headaches

rapid heartbeat

feeling more thirsty or hungry than usual

 voice changes and gets deeper and lower • changes in mood or behavior, such as decreased sex drive, irritability or

decrease in your amount of urine

feeling cold

 swelling of your ankles loss of appetite Skin problems.

skin blistering or skin peeling

worsening signs or symptoms, which may include: • confusion, sleepiness, memory problems, changes in mood or behavior, stiff

For treatment of non-small cell lung cancer before surgery (neoadjuvant), Getting medical treatment right away may help prevent these problems

with liver cancer with mild liver impairment (Child-Pugh A) following treatment

with liver cancer with mild liver impairment (Child-Pugh A) following treatment

• For treatment of metastatic non-small cell lung cancer that has spread to other

• OPDIVO. The doctor may treat you with corticosteroids or hormone replacement parts of your body, when OPDIVO is used in combination with ipilimumab, medicines. If the side effects are severe, the doctor may delay or completely stop

Tell your treating doctor or nurse immediately if you experience any of the • low blood pressure

recurrent or metastatic esophageal squamous cell carcinoma after prior squamous cell carcinoma, OPDIVO is given every 2 weeks or every 3 weeks

Complications of stem cell transplantation using donor stem cells • swelling (edema)

adenocarcinoma, when OPDIVO is given in combination with fluoropyrimidine may happen if the transplantation was performed either before or after treatment • dry skir and platinum containing chemotherapy, OPDIVO is given every 2 weeks or every with OPDIVO. Your treating doctor will monitor you for signs of complications if • diarrhea

> Very common side effects, affect more than 1 in 10 users: · weakness, generally feeling unwell

• swelling (edema), including swelling of the hands, ankles or feet (peripheral

difficulty swallowing

• you have received radiation treatment to your chest area in the past and have

As with any medicine, use of OPDIVO may cause side effects in some users. Do

• itchy skin, including widespread itching not be alarmed by the list of side effects. You may not suffer from any of them. erythema manifested by skin redness and inflammation pain in muscles, bones, and joints dizziness

> nasal congestion pneumonia, including pneumonia involving the bronchi

 shortness of breath, shortness of breath upon exertion decreased weight back pain low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid gland) that can cause fatigue and weight gain

gland)] that can cause rapid heart rate, sweating and weight loss · thyroid gland problems, including thyroid gland inflammation (thyroiditis) urinary tract infection · liver inflammation (hepatitis) high blood pressure high level of sugar in blood (hyperglycemia)

 numbness, pain, tingling or burning in the hands or feet (peripheral neuropathy)
 swollen stomach · abnormal laboratory test results infusion-related reactions Common side effects, affect 1-10 in 100 users: inflammation of the eye iris and ciliary body (iridocyclitis)

• inflammation of the nerves manifested by numbness, weakness, tingling, of pain accompanied by burning sensation (sensory and peripheral neuropathy intestinal perforation ulcers or sores in the mouth (stomatitis) • severe skin condition that causes red, sometimes itchy spots, similar to the

rash of measles, which starts on the limbs and sometimes on the face and the rest of the body (erythema multiforme) • severe inflammation of the skin manifested by redness and peeling of extensive skin areas (exfoliative dermatitis)

• accumulation of fluid in the pleural cavity around the lungs (pleural effusion) which may cause shortness of breath and sometimes also chest pain and fever pulmonary embolism (blood clot in the lungs) . inflammation of the lung tissues (pneumonitis) characterized by coughing and difficulty breathing, shortness of breath and cough

• interstitial lung disease characterized by shortness of breath and dry cough, and causing lung scarring • respiratory failure (extreme difficulty breathing) acute renal injury sepsis general health condition deterioration

 intestinal obstruction (small intestine obstruction) inflammation of the colon (colitis) liver problems dry skin swollen stomach (abdomen) due to fluid accumulation (ascites)

bleeding from esophageal varices

 death due to side effects paralysis of the fibular nerve in the leg characterized by pain in the calf,
 pneumonia decreased sensation or numbness, muscle weakness, and in severe cases • severe allergic reaction (anaphylactic reaction) foot drop or typical limping (peroneal nerve palsy)

 respiratory tract infection muscles pain, muscles weakness not due to exercise (myopathy) muscles inflammation (myositis) Siogren's syndrome, a disease in whice

(spondyloarthropathy) Uncommon side effects, affect 1-10 patients in 1000 users: • adrenal glands insufficiency (decrease in the level of hormones secreted by adrenal glands located above the kidneys) sudden death

septic shock

feeling tired

 itching, including widespread itching gastrointestinal bleeding hair loss decreased appetite esophageal fistula Side effects occurring when OPDIVO is administered in combination with Very common side effects, affect more than 1 in 10 users

 abnormal laboratory test results Common side effects, affect 1-10 in 100 users: pneumonia • fever due to low level of neutrophils, a type of white blood cell (febrile neutropenia) acute kidney injury

• stomach-area (abdominal) pain

sores or ulcers in the mouth (stomatitis)

• rash, redness, pain, swelling or blistering of the hands or feet

• inflammation of the lung tissues (pneumonitis) characterized by coughing and • stomach-area (abdominal) pain difficulty breathing, shortness of breath and cough • respiratory failure (extreme difficulty breathing) • swollen stomach (abdomen) due to fluid accumulation (ascites) death due to side effects Side effects occurring when OPDIVO is administered in combination with cabozantinib include Very common side effects, affect more than 1 in 10 users:

nausea

dvspepsia

liver toxicity

feeling tired or weak

high blood pressure

leaflet of ipilimumab.

For combined treatment with OPDIVO and cabozantinib, see also patient

These are not all the possible side effects of OPDIVO. For medical information

Side effects can be reported to the Ministry of Health by clicking on the "Reporting

(www.health.gov.il) that directs you to the online form for reporting side effects, or

· Avoid poisoning! This medicine, and all other medicines, must be stored in

a safe place out of the reach and sight of children and/or infants, in order to

avoid poisoning. Do not induce vomiting unless explicitly instructed to do so

• Do not use the medicine after the expiry date (exp. date) that appears on the

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

• Storage conditions: Refrigerate at 2°C-8°C. Protect from light by storing the

If you experience any side effect, if any side effect gets worse, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor

side effects following drug treatment" link found on the Ministry of Health homep

hrough the following link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

vial in the original package until time of use.

immune system activity"

 inflammation of the colon (colitis) pain in muscles, bones, and joints cough, cough with phleam • shortness of breath, shortness of breath upon exertion pneumonia • upper respiratory tract infection • inflammation of the lung tissues (pneumonitis) characterized by coughing and • liver problems. See "Liver problems" in section "Severe side effects related to

 decreased appetite headache dizziness flu-like illness weakness, generally feeling unwell

difficulty breathing, shortness of breath and cough

ulcers or sores in the mouth (stomatitis)

constipation

• low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid low blood pressure gland)] that can cause fatigue and weight gain • low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid
• pain in muscles, bones and joins gland)] that can cause fatigue and weight gain • high thyroid hormone levels [hyperthyroidism (increased activity of the thyroid
• change in the sense of taste gland)] that can cause rapid heart rate, sweating and weigh loss adrenal glands insufficiency (decrease in the level of hormones secreted by

adrenal glands located above the kidneys) · voice disorders (difficulty speaking due to disorders of the pharynx, vocal cords, tongue or mouth) • upper respiratory tract infection · abnormal laboratory test results · abnormal laboratory test results Common side effects, affect 1-10 in 100 users: Common side effects, affect 1-10 in 100 users: • vitiligo, a disease in which light patches appear on the skin

 pneumonia high blood pressure pulmonary embolism (blood clot in the lungs) • high level of sugar in blood (hyperglycemia) • inflammation of the lung tissues (pneumonitis) characterized by coughing and intestinal perforation difficulty breathing, shortness of breath and cough accumulation of fluid in the pleural cavity around the lungs (pleural effusion) · urinary tract infection which may cause shortness of breath and sometimes also chest pain and fever Uncommon side effects, affect 1-10 in 1000 users: pulmonary embolism (blood clot in the lungs)

• inflammation of the pituitary gland (hypophysitis) Side effects occurring when OPDIVO is administered in combination with chemotherapy containing fluoropyrimidine and platinum include:
Very common side effects, affect more than 1 in 10 users: acute kidnev iniurv hepatic event numbness, pain, tingling or burning in the hands or feet (peripheral neuropathy) abnormal liver function

 bleeding from esophageal varices death due to side effects diarrhea muscle pain, muscle weakness not caused by exercise (myopathy muscles inflammation (myositis) difficulty swallowing stomach-area (abdominal pain) • paralysis of the fibular nerve in the leg characterized by pain in the calf.

decreased sensation or numbness, muscle weakness, and in severe cases ulcers or sores in the mouth (stomatitis) foot drop or typical limping (peroneal nerve palsy) feeling tired Sjogren's syndrome, a disease in which the immune system attacks mainly swelling (edema) chronic joints inflammation usually involving the spinal joints

 decreased appetite decreased weight numbness, pain, tingling or burning in the hands or feet (peripheral • pain in muscles, bones and joints • infusion-related reactions rash itching Uncommon side effects, affect 1-10 in 1000 users: hair loss · inflammation of the brain (encephalitis)

 rash, redness, pain, swelling or blistering of the hands or feet muscle inflammation leading to necrosis · cough, cough with phlegm • eye pain and redness - inflammation of the uvea (uveitis) upper respiratory tract infection Side effects occurring when OPDIVO is administered in combination with pneumonia chemotherapy include: Very common side effects, affect more than 1 in 10 users: difficulty sleeping · abnormal laboratory test results feeling tired Common side effects, affect 1-10 in of 100 users: · generally feeling unwell

• fever due to low level of neutrophils, a type of white blood cells (febrile constipation inflammation of the lung tissues (pneumonitis) characterized by coughing and difficulty breathing, shortness of breath and cough decreased appetite • low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid gland)] that can cause fatigue and weight gain

 numbness, pain, tingling or burning in the hands or feet (peripheral neuropathy) · abnormal laboratory test results death due to side effects Common side effects, affect 1-10 in 100 users: For combined treatment with OPDIVO and ipilimumab, see also patient

 acute kidney injury Side effects occurring when OPDIVO is administered in combination with ipilimumab and chemotherapy include ery common side effects, affect more than 1 in 10 users: on side effects, contact your treating doctor.

• pain in muscles, bones, and joints diarrhea constination • stomach-area (abdominal) pain

 shortness of breath • low thyroid hormone levels [hypothyroidism (decreased activity of the thyroid gland)] that can cause fatigue and weight gain

 Do not freeze or shake. • Once the infusion has been prepared: complete administration of the infusion immediately, OPDIVO can be stored after preparation:

o at room temperature (20°C-25°C) and room light for a period of no more than 8 hours (out of the 7 days) from the time of preparation until the end of infusion administration.

of up to 7 days from the time of preparation until the end of administration. . Do not dispose of medicines via wastewater or waste bin. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment. 6. FURTHER INFORMATION:

In addition to the active ingredient, the medicine also contains: Mannitol, sodium citrate dihydrate, sodium chloride, polysorbate 80, pentetic acid and water for injection. May contain hydrochloric acid and/or sodium hydroxide. What the medicine looks like and the contents of the package: A clear to opalescent, colorless to slightly yellowish liquid. The liquid may contain

OPDIVO is available in a 10 ml (100 mg) single-use vial and a 4 ml (40 mg) single-use vial. Manufacturer's name and address: Bristol-Myers Squibb Holdings Pharma Ltd., Liability Company, Manati, Puerto Rico, USA. Registration holder's name and address: Bristol-Myers Squibb (Israel) Ltd.,

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

18 Aharon Bart St. P.O. Box. 3361, Kiryat Arye, Petach Tikva 4951448.

Revised in June 2023 according to MOH guidelines.

Preparation and Administration Visually inspect for particulate matter and discoloration. OPDIVO is a clear to palescent, colorless to pale-yellow solution. Discard if cloudy, discolored, or diluted solution if not used within 7 days from the time of preparation. refrigerated at a temperature of 2°C-8°C and protected from light for a period contains extraneous particulate matter other than a few translucent-to-white. • Do not freeze.

roteinaceous particles. Do not shake.

Dilute OPDIVO with either 0.9% Sodium Chloride Injection USP or 5% to 1.2 micrometer?

• For adult and pediatric patients with body weight 40 kg or greater, do not OWith platinum-doublet chemotherapy: administer OPDIVO first followed exceed a total volume of infusion of 160 mL. For adult and pediatric patients with body weight less than 40 kg. do not exceed a total volume of infusion of 4 mL/kg of body weight. Mix diluted solution by gentle inversion. Do not shake.

 Discard partially used vials or empty vials of OPDIVO The product does not contain a preservative. After preparation, store the diluted solution either:

• at room temperature and room light for no more than 8 hours from the time of preparation to end of the infusion. Discard diluted solution if not used within 8 hours from the time of preparation; or

מידע לצוות הרפואי معلومات للطاقم الطبي

Information for Healthcare professionals under refrigeration at 2°C to 8°C (36°F to 46°F) and protected from light fo no more than 7 days from the time of preparation to end of infusion. Discard

 Administer the infusion, after dilution, over 30 minutes or 60 minutes • Withdraw the required volume of OPDIVO and transfer into an intravenous depending on the dose through an intravenous line containing a sterile non-pyrogenic, low protein binding in-line filter (pore size of 0.2 micromete

Dextrose Injection, USP to prepare an infusion with a final concentration

• Administer OPDIVO in combination with other therapeutic agents as follows: ranging from 1 mg/mL to 10 mg/mL. The total volume of infusion must not

With ipilimumab: administer OPDIVO first followed by ipilimumab on the

by platinum doublet chemotherapy on the same day.

With ipilimumab and platinum-doublet chemotherapy: administer OPDIV first followed by ipilimumab and then platinum-doublet chemotherapy of the same day. With fluoropyrimidine- and platinum-containing chemotherapy: administe OPDIVO first followed by fluoropyrimidine- and platinum-containing

chemotherapy on the same day. Use separate infusion bags and filters for each infusion. Flush the intravenous line at end of infusion.

• Do not co-administer other drugs through the same intravenous line.

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