Subcutaneous administration is now available for the following indications:[1]

PrOPDIVO® SC, indicated for:

- In monotherapy, for the treatment of adult patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer after:
  – prior fluoropyrimidine-based therapy in combination with oxaliplatin or irinotecan following treatment with intravenous nivolumab and ipilimumab.
- The adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC.

The above indications have been issued market authorization **with conditions**, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for PrOPDIVO® SC please refer to Health Canada's Notice of Compliance with conditions - drug products website: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions.html.

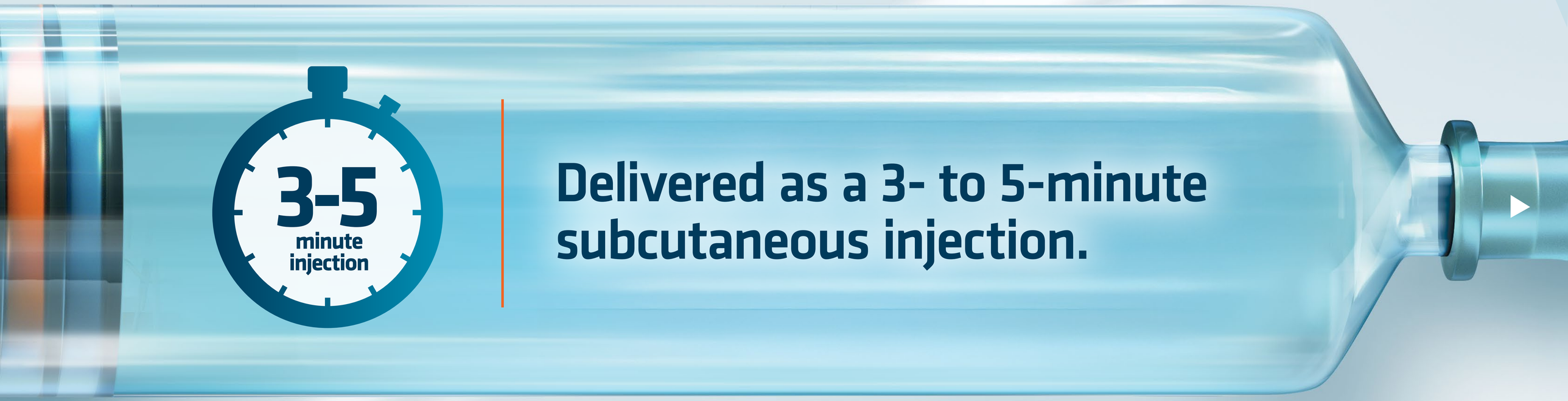
PrOPDIVO® SC, indicated for:

- Advanced or metastatic renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.
- Intermediate/poor-risk advanced or metastatic RCC following treatment with intravenous nivolumab and ipilimumab.
- The first-line treatment of adult patients with advanced (not amenable to curative surgery or radiation therapy) or metastatic RCC, when used in combination with cabozantinib.
- Unresectable or metastatic melanoma who have not received prior systemic therapy for unresectable or metastatic melanoma, as monotherapy.
- Unresectable or metastatic melanoma who have not received prior systemic therapy for unresectable or metastatic melanoma, as monotherapy following treatment with intravenous nivolumab and ipilimumab.
- Unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.
- Melanoma with regional lymph node involvement, in transit metastases/satellites without metastatic nodes, or distant metastases, as adjuvant therapy after complete resection.
- Adjuvant treatment of adult patients with Stage IIB or IIC melanoma following complete resection.
- Locally advanced or metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have disease progression on a therapy for these aberrations prior to receiving OPDIVO SC.
- Recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) progressing on or after platinum-based therapy.
- Adjuvant treatment of completely resected esophageal or gastroesophageal junction (GEJ) cancer in patients who have residual pathologic disease following prior neoadjuvant chemoradiotherapy (CRT).
- HER2 negative advanced or metastatic gastric cancer, gastroesophageal junction cancer or esophageal adenocarcinoma (GC/GEJC/EAC), in combination with fluoropyrimidine- and platinum-containing chemotherapy.
- Unresectable or metastatic ESCC in adult patients with tumour cell PD-L1 expression ≥1% as determined by a validated test, and no prior systemic therapy for metastatic ESCC, when used in combination with fluoropyrimidine- and platinum-containing chemotherapy.
- Neoadjuvant treatment of adult patients with resectable NSCLC (tumours ≥4 cm or node positive) when used in combination with platinum-doublet chemotherapy.
- Unresectable or metastatic urothelial carcinoma in adult patients, as first-line treatment in combination with cisplatin and gemcitabine.

The above indications have been issued market authorization without conditions.

Pr OPDIVO® SC
subcutaneous nivolumab for injection

Nivolumab is now available for subcutaneous injection



Delivered as a 3- to 5-minute subcutaneous injection.

Please consult the OPDIVO SC Product Monograph for important information relating to:

- The most serious warnings and precautions regarding severe/fatal immune-mediated adverse reactions (imARs), allogeneic hematopoietic stem cell transplantation (HSCT), multiple myeloma and administration under the supervision of physicians experienced in the treatment of cancer.
- Other relevant warnings and precautions regarding frequency and signs and symptoms of imARs, infusion reaction, patients on controlled sodium diet, caution when driving or operating a vehicle or potentially dangerous machinery, haemophagocytic lymphohistiocytosis (HLH), pregnancy, nursing and patients with moderate or severe hepatic or severe renal impairment.
- Conditions of clinical use, adverse reactions, drug interactions, and dosing instructions.

The Product Monograph is also available by calling us at: 1-866-463-6267.

About OPDIVO SC[1]

- Administered by an HCP
- Single SC injection given every 2, 3 or 4 weeks
- Administered into the abdomen or thigh
- Fixed-dose, ready-to-use solution
- Administered as a 3- to 5-minute subcutaneous injection
- Stable for 7 days in the syringe (when stored at 2 °C to 8 °C)

CHECKMATE-67T trial: OPDIVO SC 1200 mg demonstrated noninferiority exposures to OPDIVO i.v. 3 mg/kg[1,2]*

CHECKMATE-67T study design for OPDIVO SC

CHECKMATE-67T: Multicenter, randomized, open-label study

Patients ≥18 years of age with histologically confirmed advanced or metastatic renal cell carcinoma with a clear cell component, including those with sarcomatoid features, and who received no more than 2 prior systemic treatment regimen (N=495)

OPDIVO SC (n=248)

OPDIVO i.v. (n=247)

Primary objective (co-primary endpoints):

Demonstrate noninferiority defined by:

- Model-predicted serum concentration over 28 days (Cavgd28)
- Minimum serum concentration at steady state (Cminss)

Secondary objective:

Demonstrate noninferiority of the overall response rate (ORR)

* CHECKMATE-67T was a multicenter, randomized, open-label study in patients with advanced or metastatic clear cell renal cell carcinoma. A total of 495 patients were randomized to receive either OPDIVO SC (n=248) or intravenous nivolumab (n=247). The primary objective of the study was to demonstrate noninferiority of the model-predicted serum nivolumab concentration over 28 days (Cavgd28) and minimum serum concentration at steady state (Cminss) as co-primary endpoints for the subcutaneous administration of OPDIVO SC to the intravenous administration of nivolumab. The secondary objective of the study was to demonstrate noninferiority of the overall response rate (ORR) for the subcutaneous administration of OPDIVO SC to the intravenous administration of nivolumab, as assessed by blinded independent central review (BICR).

CHECKMATE-67T trial results

OPDIVO SC 1200 mg demonstrated noninferiority exposures to OPDIVO i.v. 3 mg/kg[1,2]*

	OPDIVO SC	OPDIVO i.v.	GMR
Model-predicted time-averaged serum concentration over 28 days (Cavgd28)	77.4 µg/mL	36.9 µg/mL	2.09 (90% CI: 2.00, 2.20)
Model-predicted minimum serum concentration at steady state (Cminss)	122.2 µg/mL	68.9 µg/mL	1.77 (90% CI: 1.63, 1.93)

NOTE: PK PARAMETERS ARE FROM POPULATION PHARMACOKINETICS MODEL.

Based on Population Pharmacokinetics analysis, OPDIVO SC PK can be described with first order absorption from the extravascular compartment and time-varying CL. Steady state is achieved after 16 weeks and the average systemic accumulation ratio was 2.3.

Use of OPDIVO SC is supported by evidence from clinical studies conducted with OPDIVO i.v., and additional pharmacokinetic and safety data that demonstrated **comparable pharmacokinetics and safety profiles between OPDIVO SC and OPDIVO i.v.**[1]

Please see the separate Product Monograph for OPDIVO (i.v. formulation) for more information.

Exploratory efficacy analysis

Descriptive results of BICR-assessed ORR were: 24% (60/248; 95% CI: 19, 30) for OPDIVO SC; 18% (45/247; 95% CI: 13.6, 23.6) for OPDIVO i.v. (secondary endpoint).

CI: confidence interval; CL: clearance at steady state; GMR: geometric mean ratio; PK: pharmacokinetics.

* CHECKMATE-67T was a multicenter, randomized, open-label study in patients with advanced or metastatic clear cell renal cell carcinoma. A total of 495 patients were randomized to receive either OPDIVO SC (n=248) or intravenous nivolumab (n=247). The primary objective of the study was to demonstrate noninferiority of the model-predicted serum nivolumab concentration over 28 days (Cavgd28) and minimum serum concentration at steady state (Cminss) as co-primary endpoints for the subcutaneous administration of OPDIVO SC to the intravenous administration of nivolumab. The secondary objective of the study was to demonstrate noninferiority of the overall response rate (ORR) for the subcutaneous administration of OPDIVO SC to the intravenous administration of nivolumab, as assessed by blinded independent central review (BICR).

Established safety profile[1,2]

- Patients received OPDIVO SC every 4 weeks (n=247) or OPDIVO i.v. every 2 weeks (n=245).
- Median duration of treatment was 6.6 months (range 0 to 22.4).

	OPDIVO SC (n=247)
Serious adverse events	27.9%
Adverse event leading to discontinuation	9.3%
Adverse event leading to dose interruption	34.4%
Grade 3-5 adverse events	36.4%
Fatal adverse reactions (myocarditis, myasthenia, and colitis complications)	1.2%

The most frequent serious adverse reactions in at least 1% of patients were:

- Pleural effusion
- Pneumonitis
- Hyperglycemia
- Hyperkalemia
- Diarrhea

The most common adverse reactions (≥10%) were:

- Anemia
- Fatigue
- Musculoskeletal pain
- Pruritus
- Rash
- Blood creatinine increased
- Arthralgia
- Cough

For complete safety information, please refer to the OPDIVO SC Product Monograph.

Please see the separate Product Monograph for OPDIVO (i.v. formulation) for more information.

Established safety profile[1,2] (continued)

Select adverse events in ≥5% of patients receiving OPDIVO SC[1]

	OPDIVO SC (n=247)		OPDIVO i.v. (n=245)	
Adverse reaction	**All grades (%)**	**Grades 3-4 (%)**	**All grades (%)**	**Grades 3-4 (%)**
Endocrine				
Hypothyroidism	9.7	0	12.2	0
Gastrointestinal				
Diarrhea	9.7	0.4	13.5	0.4
Abdominal pain	9.7	0	9.0	0.4
Nausea	8.1	0	9.0	0
Constipation	7.7	0	6.1	0
Vomiting	6.1	0.4	4.9	0
General				
Fatigue	19.8	2.4	24.9	3.3
Injection site reaction	6.9	0	0	0
Edema	5.7	0.4	10.6	0.8
Metabolism and nutrition				
Hyperglycemia	9.3	2.4	13.1	2.0
Decreased appetite	8.9	0	11.4	0.8
Musculoskeletal and connective tissue				
Musculoskeletal pain	20.2	1.2	29.4	2.4
Arthralgia	11.7	0.4	15.9	0.4
Skin and subcutaneous tissue				
Pruritus	16.2	0.4	21.2	0
Rash	13.4	1.2	11.8	1.2
Respiratory				
Cough	10.9	0	11.4	0

For complete safety information, please refer to the OPDIVO SC Product Monograph.

Please see the separate Product Monograph for OPDIVO (i.v. formulation) for more information.

Established safety profile[1,2] (continued)

Immune-mediated adverse reactions[1]

	OPDIVO SC (n=247)		OPDIVO i.v. (n=245)	
Adverse reaction	**All grades (%)**	**Grades 3-4 (%)**	**All grades (%)**	**Grades 3-4 (%)**
Endocrinopathies	12.6	0.8	18.0	1.2
Gastrointestinal events	6.1	0	5.3	0.4
Hepatic events	8.1	2.0	11.0	3.7
Pulmonary events	5.3	1.6	3.3	0.8
Renal events	2.8	0	4.9	0
Skin events	23.1	1.6	26.5	1.2
Hypersensitivity/ infusion reactions events	0.4	0.4	2.4	0

For complete safety information, please refer to the OPDIVO SC Product Monograph.

Please see the separate Product Monograph for OPDIVO (i.v. formulation) for more information.

Preparation and administration[1]

- OPDIVO SC should be administered by subcutaneous injection only, using the doses specified. It is not intended for intravenous administration. OPDIVO SC should be administered by a healthcare professional.
- OPDIVO SC is a single-use, ready-to-use solution for injection. It should not be diluted.
- Prior to use, visually inspect for particulate matter and discolouration. OPDIVO SC is a clear to opalescent, colourless to yellow solution. Discard if the solution is discoloured or contains extraneous particulate matter other than a few translucent-to-white particles. Do not shake.

Preparation[1]

OPDIVO SC is compatible with polypropylene, polycarbonate, polyethylene, polyurethane, polyvinyl chloride, fluorinated ethylene propylene, and stainless steel.

1

A syringe, a transfer needle and a hypodermic injection needle are needed to withdraw OPDIVO SC from the vial.

2

OPDIVO SC may be injected using a 23G-25G (3/8”-5/8”) hypodermic injection needle or winged butterfly needle.

3

If the syringe was stored in a refrigerator, allow OPDIVO SC vial(s) to reach room temperature prior to administration.

4

Withdraw the appropriate fixed-dose OPDIVO SC into a single syringe.

Dosage of OPDIVO SC	Vials of OPDIVO SC needed	Total of OPDIVO SC to withdraw
600 mg	1	5 mL
900 mg	2	7.5 mL
1,200 mg	2	10 mL

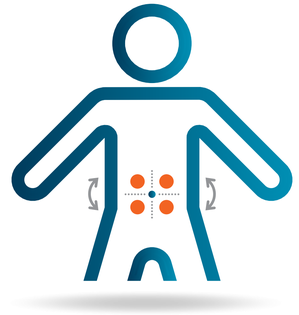
5

Discard any unused solution remaining in the vial.

Preparation and administration[1] (continued)

Administration[1]

Administer the full contents of the syringe into the subcutaneous tissue of the abdomen or thigh over a period of 3 to 5 minutes.



Alternate injection sites for successive injections.

Do not inject into areas where the skin is tender, red, or bruised, or areas where there are scars or moles.

If the administration of OPDIVO SC is interrupted, continue administering at the same site, or at an alternate site.

During treatment with OPDIVO SC, do not administer other subcutaneous medications at the same site used for OPDIVO SC.

Storage of prepared syringe[1]

OPDIVO SC should be used immediately once withdrawn into the syringe.

- If not used immediately, the syringe can be stored in the refrigerator at 2 °C to 8 °C, protected from light for up to 7 days and/or at room temperature 15 °C to 25 °C and room light for up to 8 hours.
- Discard if storage time exceeds these limits. Do not freeze.

Recommended doses[1]

As monotherapy	Indications	Duration of therapy
 **600 mg OPDIVO SC Q2W** **OR**  **1,200 mg OPDIVO SC Q4W**	■ Unresectable or metastatic melanoma ■ Metastatic non-small cell lung cancer ■ Advanced or metastatic renal cell carcinoma ■ Squamous cell carcinoma of the head and neck	As long as clinical benefit is observed or until disease progression or unacceptable toxicity.
	■ Adjuvant treatment of melanoma (Stage III/IV) ■ Adjuvant treatment of melanoma (Stage IIB/IIC) ■ Adjuvant treatment of urothelial carcinoma ■ Adjuvant treatment of resected esophageal or gastroesophageal junction	As long as clinical benefit is observed or until disease recurrence or unacceptable toxicity for up to 1 year.

As monotherapy following combination with YERVOY	Indications	Duration of therapy
 **600 mg OPDIVO SC Q2W** **OR**  **1,200 mg OPDIVO SC Q4W**	■ Unresectable or metastatic melanoma ■ Advanced or metastatic renal cell carcinoma ■ Microsatellite instability-high (MSI-H)/ mismatch repair deficient (dMMR) metastatic colorectal cancer	Until disease progression or unacceptable toxicity.

For complete information on dosing, please refer to the OPDIVO SC Product Monograph.

Q2W: every 2 weeks; Q3W: every 3 weeks; Q4W: every 4 weeks.

Recommended doses[1] (continued)

In combination with other therapeutic agents	Indications	Duration of therapy
 **600 mg OPDIVO SC Q2W** **OR**  **1,200 mg OPDIVO SC Q4W** **+ cabozantinib**	■ Advanced or metastatic renal cell carcinoma	Until disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression.
 **600 mg OPDIVO SC Q2W** **OR**  **900 mg OPDIVO SC Q3W** **+ fluoropyrimidine- and platinum-containing chemotherapy**	■ Gastric cancer, gastro-esophageal junction cancer or esophageal adenocarcinoma	Until disease progression, unacceptable toxicity, or up to 2 years.
 **600 mg OPDIVO SC Q2W** **OR**  **1,200 mg OPDIVO SC Q4W** **+ fluoropyrimidine- and platinum-containing chemotherapy**	■ Unresectable or metastatic esophageal squamous cell carcinoma	Until disease progression, unacceptable toxicity, or up to 2 years.

For complete information on dosing, please refer to the OPDIVO SC Product Monograph.

Q2W: every 2 weeks; Q3W: every 3 weeks; Q4W: every 4 weeks.

Recommended doses[1] (continued)

In combination with other therapeutic agents	Indications	Duration of therapy
 **900 mg OPDIVO SC Q3W** **+ platinum-doublet chemotherapy**	■ Neoadjuvant treatment of resectable non-small cell lung cancer	3 cycles.
 **900 mg OPDIVO SC Q3W** **+ cisplatin and gemcitabine** **followed by**  **600 mg OPDIVO SC Q2W** **OR**  **1,200 mg OPDIVO SC Q4W**	■ First-line treatment of unresectable or metastatic urothelial carcinoma	In combination with cisplatin and gemcitabine for up to 6 cycles. After completing combination therapy, administer OPDIVO SC as monotherapy, until disease progression, unacceptable toxicity, or up to 2 years from first dose.

For complete information on dosing, please refer to the OPDIVO SC Product Monograph.

Q2W: every 2 weeks; Q3W: every 3 weeks; Q4W: every 4 weeks.

OPDIVO SC is now available: Consider nivolumab for subcutaneous administration

Demonstrated comparable pharmacokinetics profile between OPDIVO SC and OPDIVO i.v.[1]

- **CHECKMATE-67T trial:** OPDIVO SC 1200 mg demonstrated noninferiority exposures to OPDIVO i.v. 3 mg/kg*
  - **Geometric mean of Cavgd28** was **77.4 ug/mL** (90% CI: 74.55, 80.30) for OPDIVO SC (n=242) vs. **36.9 ug/mL** (90% CI: 35.56, 38.23) for OPDIVO i.v. (n=245), with a GMR of 2.09 (90% CI: 2.00, 2.20)
  - **Geometric mean of Cminss** was **122.2 ug/mL** (90% CI: 114.55, 130.42) for OPDIVO SC (n=242) vs. **68.9 ug/mL** (90% CI: 64.68, 73.40) for OPDIVO i.v. (n=245), with a GMR of 1.77 (90% CI: 1.63, 1.93)

Exploratory efficacy analysis[1]

- Descriptive results of **BICR-assessed ORR** were: **24%** (60/248; 95% CI: 19, 30) for OPDIVO SC; **18%** (45/247; 95% CI: 13.6, 23.6) for OPDIVO i.v. (secondary endpoint)*

Established safety profile[1]

- The most common adverse reactions (≥10%) were anemia, fatigue, musculoskeletal pain, pruritus, rash, blood creatinine increased, arthralgia, and cough

Fast administration[1]

- OPDIVO SC is administered as a 3- to 5-minute subcutaneous injection

BICR: blinded independent central review; CI: confidence interval; GMR: geometric mean ratio; ORR: overall response rate.

* CHECKMATE-67T was a multicenter, randomized, open-label study in patients with advanced or metastatic clear cell renal cell carcinoma. A total of 495 patients were randomized to receive either OPDIVO SC (n=248) or intravenous nivolumab (n=247). The primary objective of the study was to demonstrate noninferiority of the model-predicted serum nivolumab concentration over 28 days (Cavgd28) and minimum serum concentration at steady state (Cminss) as co-primary endpoints for the subcutaneous administration of OPDIVO SC to the intravenous administration of nivolumab. The secondary objective of the study was to demonstrate noninferiority of the overall response rate (ORR) for the subcutaneous administration of OPDIVO SC to the intravenous administration of nivolumab, as assessed by blinded independent central review (BICR).

Important safety information[1]

Clinical use:

Efficacy and safety not established in pediatric patients.

Most serious warnings and precautions:

Severe/fatal immune-mediated adverse reactions (imARs): OPDIVO SC as monotherapy can cause severe and fatal immune-mediated adverse reactions, including pneumonitis, interstitial lung disease, encephalitis, myocarditis, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and autoimmune hemolytic anemia. Immune-mediated adverse reactions may involve any organ system. Onset may occur during treatment or months after the last dose. Early diagnosis and appropriate management are essential to minimize potential life-threatening complications. Monitor patients for signs and symptoms of imARs and appropriately manage with treatment modifications. Permanently discontinue for any severe imARs that recur and for any life-threatening imARs.

Administration: Administer OPDIVO under the supervision of physicians experienced in the treatment of cancer.

Allogeneic hematopoietic stem cell transplantation (HSCT): Complications, including fatal events, occurred in patients who received allogeneic HSCT after OPDIVO. Preliminary results from the follow-up of patients undergoing allogeneic HSCT after previous exposure to nivolumab showed a higher than expected number of cases of acute graft-versus-host disease (GVHD) and transplant-related mortality. Complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT. Follow patients closely for early evidence of transplant-related complications such as hyperacute GVHD, severe (Grades 3 to 4) acute GVHD, steroid-requiring febrile syndrome, hepatic venoocclusive disease (VOD), and other immune-mediated adverse reactions, and intervene promptly.

Multiple myeloma: Increased mortality in patients with multiple myeloma [not an approved indication] when OPDIVO is added to a thalidomide analogue and dexamethasone. Treatment of patients with multiple myeloma with a PD-1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.

Other relevant warnings and precautions:

- Severe cases of these imARs have been observed, including fatal cases. Monitor patients for signs and symptoms of:
  - Cardiac adverse events and pulmonary embolism with combination therapy
  - Endocrinopathies, including hypothyroidism, hyperthyroidism, hypoparathyroidism, adrenal insufficiency, hypophysitis, diabetes mellitus, and diabetic ketoacidosis
  - Diarrhea, additional symptoms of colitis, and cytomegalovirus (CMV) infection/reactivation
  - Hepatotoxicity, including hepatitis
  - Pneumonitis or interstitial lung disease
  - Nephrotoxicity, including nephritis and renal failure
  - Rash, Stevens-Johnson syndrome, toxic epidermal necrolysis
  - Encephalitis
  - Aplastic anemia
  - Myelitis (including transverse myelitis)
  - Autoimmune hemolytic anemia
  - Myotoxicity (myositis, myocarditis, and rhabdomyolysis)
  - Other imARs, including solid organ transplant rejection and rapid-onset and severe graft-versus-host disease (GVHD)
- Infusion reaction
- Patients on controlled sodium diet
- Caution when driving or operating a vehicle or potentially dangerous machinery
- Haemophagocytic lymphohistiocytosis (HLH)
- Effective contraception in women of reproductive potential
- Pregnancy and nursing women
- Has not been studied in patients with moderate or severe hepatic or severe renal impairment

For more information:

Please consult the OPDIVO SC Product Monograph for important information relating to adverse reactions, drug interactions, and dosing, which have not been discussed in this piece.
The Product Monograph is also available by calling us at: 1-866-463-6267.

References:

1. OPDIVO SC Product Monograph. Bristol-Myers Squibb Canada. **2.** Albiges L *et al*. Subcutaneous versus intravenous nivolumab for renal cell carcinoma. *Ann Oncol*. 2025;36(1):99-107.

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