Dimensions: 210mm x 297mm

This brochure was created based on the most updated data presented in the latest CCDS (CCDS-MK3475-IV-102019a) at the time of creation of the job. All data must be updated with data from the locally approved PI.

Note: In accordance with Corporate Policy 4 (Customer Facing, Marketing & Business Practices) and the Worldwide Review Guidelines (WRG), SSI must be included to ensure appropriate communication of safety considerations.

Local SSI is created at the local level based on the approved local product circular. (If available, approved SSI based on the US product circular can be used as a springboard for that activity.)

Please refer to the WRG for specific requirements.

KEYTRUDA™
(pembrolizumab) Injection 100 mg

Align to local label.

Your KEY to managing treatment with **KEYTRUDA™**

A guide for providers

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

Footline should be customized at the local level, based on local guidelines.

Table of Contents

This resource is intended to help you guide your patients through treatment with the anti–PD-1 therapy KEYTRUDA.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™
(pembrolizumab) Injection 100 mg

CCDS: p3A,B

CCDS: p3C-F

CCDS: p3G

CCDS: p3H,I

CCDS: p4A

CCDS: p4B

CCDS: p4C

Approved indications for KEYTRUDA™

Melanoma

- KEYTRUDA (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.
- KEYTRUDA is indicated for the adjuvant treatment of patients with melanoma with lymph node involvement who have undergone complete resection.

Non–Small Cell Lung Carcinoma

- KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung carcinoma (NSCLC), with no EGFR or ALK genomic tumor aberrations.
- KEYTRUDA, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
- KEYTRUDA as monotherapy is indicated for the first-line treatment of patients with locally advanced or metastatic NSCLC whose tumors express PD-L1 with a ≥1% tumor proportion score (TPS) as determined by a validated test, with no EGFR or ALK genomic tumor aberrations.
- KEYTRUDA as monotherapy is indicated for the treatment of patients with advanced NSCLC whose tumors express PD-L1 with a ≥1% TPS as determined by a validated test and who have received platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have received prior therapy for these aberrations prior to receiving KEYTRUDA.

Small Cell Lung Cancer

- KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic small cell lung cancer (SCLC) who have received two or more prior lines of therapy.

Head and Neck Squamous Cell Carcinoma

- KEYTRUDA, as a single agent or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy, is indicated for the first-line treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC).
- KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

Classical Hodgkin Lymphoma

- KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after 3 or more prior lines of therapy.

Primary Mediastinal B-Cell Lymphoma

- KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal B-cell lymphoma (PMBCL), or who have relapsed after 2 or more prior lines of therapy.

Urothelial Carcinoma

- KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (CPS ≥10) as determined by a validated test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.
- KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have received platinum-containing chemotherapy.

High-Risk Non-muscle Invasive Bladder Cancer

- KEYTRUDA is indicated for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in-situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

Gastric Cancer

- KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by a validated test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu targeted therapy.

Esophageal Cancer

- KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic esophageal cancer whose tumors express PD-L1 (CPS ≥10) as determined by a validated test, and who have received one prior line of systemic therapy.
- KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic esophageal cancer who have received two or more prior lines of systemic therapy.

Microsatellite Instability-High Cancer

- KEYTRUDA is indicated for the treatment of patients with advanced microsatellite instability-high (MSI-H), including mismatch repair deficient (dMMR), cancer who have received prior therapy.

Hepatocellular Carcinoma

- KEYTRUDA is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with an anti-angiogenic tyrosine kinase inhibitor (TKI).

Cervical Cancer

- KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by a validated test, with disease progression on or after chemotherapy.

Renal Cell Carcinoma

- KEYTRUDA, in combination with axitinib, is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1; CPS = combined positive score; HER2/neu = human epidermal growth factor receptor 2.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

CCDS: p4C

CCDS: p4D

CCDS: p4E

CCDS: p4F

CCDS: p4G

CCDS: p4H

CCDS: p5A

Selected Safety Information

[Country to add safety information based on local label]

[Country to add safety information based on local label]

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™
(pembrolizumab) Injection 100 mg

CCDS: p82A

CCDS: p9B-F; p10A-F; p11A-F; p12A

CCDS: p82A

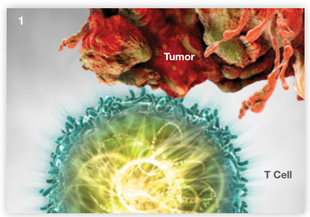
CCDS: p82A,C; p85C

CCDS: p82A; p9B-F; p10A-F; p11A-F; p12A

KEYTRUDA™: PD-1 receptor blockade

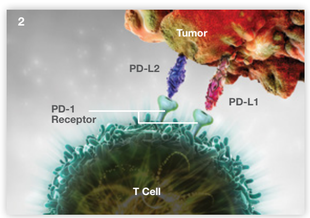
KEYTRUDA binds to the PD-1 receptor, blocking both immune-suppressing ligands, PD-L1 and PD-L2, from interacting with PD-1 to help reactivate T-cell response and immune response

Restoring active T-cell response could affect both normal healthy cells and tumor cells



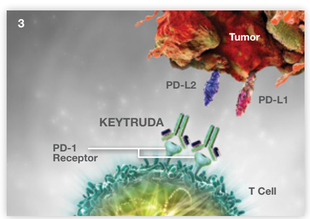
Normal immune response

When functioning properly, T cells are activated and can attack tumor cells.



Tumor evasion and T-cell deactivation

Some tumors can evade the immune system through the PD-1 pathway. The PD-L1 and PD-L2 ligands on tumors can bind with PD-1 receptors on T cells to inactivate the T cells.



T-cell reactivation with KEYTRUDA

KEYTRUDA binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, which helps restore the immune response. While having an effect on the tumor, this could also affect normal healthy cells.

PD-1 = programmed death receptor-1; PD-L2 = programmed death ligand 2.

Preparation and administration of KEYTRUDA

Preparation and administration

PREPARATION

- Protect from light. Do not freeze. Do not shake.
- Allow the vial of KEYTRUDA to come to room temperature.
- Prior to dilution, the vial of liquid can be out of refrigeration (temperatures at or below 25°C) for up to 24 hours.
- Inspect for particulate matter and discoloration prior to administration. Discard the vial if visible particles are observed.
- Withdraw the required volume up to 4 mL (100 mg) of KEYTRUDA and transfer into an intravenous bag containing 0.9% sodium chloride or 5% glucose (dextrose) to prepare a diluted solution with a final concentration ranging from 1 to 10 mg/mL. Mix diluted solution by gentle inversion.
- Discard any unused portion left in the vial.

STORAGE

- Do not freeze the infusion solution.
- The product does not contain preservative.
- The reconstituted and/or diluted product should be used immediately.
- If not used immediately, reconstituted and diluted solutions of KEYTRUDA solutions may be stored at room temperature for a cumulative time of up to 6 hours. Reconstituted and diluted solutions of KEYTRUDA may also be stored under refrigeration at 2°C to 8°C; however, the total time from reconstitution of KEYTRUDA to completion of infusion should not exceed 96 hours. If refrigerated, allow the vials and/or intravenous bags to come to room temperature prior to use.

ADMINISTRATION

- Administer infusion solution intravenously over 30 minutes using a sterile, non-pyrogenic, low-protein binding 0.2 to 5 µm in-line or add-on filter.
- Do not co-administer other drugs through the same infusion line.
- Discard any unused portion left in the vial.

CCDS: p8B-D

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

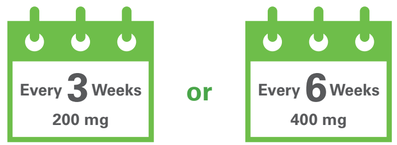
KEYTRUDA™ (pembrolizumab) Injection 100 mg

Dosing with KEYTRUDA™

Treating your patients with KEYTRUDA

The flexibility of Q3W or Q6W dosing across monotherapy indications

Choose the appropriate dosing regimen for your practice and patients



Short-interval Dosing

or

Long-interval Dosing

Both dosing options are administered as an intravenous infusion

over 30 minutes

CCDS: p5D; p6A
Calc: 52 weeks/6 infusions = 8.66 infusions per year

Fewer infusions with Q6W dosing

- The flexible dosing regimen with KEYTRUDA is an opportunity to reduce the frequency of treatments for your patients.
- Q6W dosing means fewer infusions.

Note to countries: Countries should include all monotherapy indications as appropriate and required by local regulatory regulations.

Q3W = every 3 weeks; Q6W = every 6 weeks.

Use of KEYTRUDA in specific populations

In patients with cHL or PMBCL, with Grade 4 hematological toxicity, KEYTRUDA should be withheld until adverse reactions recover to Grades 0–1.

In patients with RCC being treated with KEYTRUDA in combination with axitinib:

- If ALT or AST ≥3 times ULN but <10 times ULN without concurrent total bilirubin ≥2 times ULN, withhold both KEYTRUDA and axitinib until these adverse reactions recover to Grades 0–1. Consider corticosteroid therapy. Consider rechallenge with a single drug or sequential rechallenge with both drugs after recovery. If rechallenging with axitinib, consider dose reduction as per the axitinib prescribing information.
- If ALT or AST ≥10 times ULN or >3 times ULN with concurrent total bilirubin ≥2 times ULN, permanently discontinue both KEYTRUDA and axitinib and consider corticosteroid therapy.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; ULN = upper limit of normal.

CCDS: p7F; p8A

Use of KEYTRUDA in specific populations

- **Pregnancy**: There are no data on the use of KEYTRUDA in pregnant women. Animal reproduction studies have not been conducted with KEYTRUDA; however, blockade of PD-L1 signaling has been shown in murine models of pregnancy to disrupt tolerance to the fetus and to result in an increase in fetal loss. These results indicate a potential risk, based on its mechanism of action, that administration of KEYTRUDA during pregnancy could cause fetal harm, including increased rates of abortion or stillbirth. Human IgG4 (immunoglobulin) is known to cross the placental barrier and KEYTRUDA is an IgG4; therefore, KEYTRUDA has the potential to be transmitted from the mother to the developing fetus. KEYTRUDA is not recommended during pregnancy unless the clinical benefit outweighs the potential risk to the fetus. Women of childbearing potential should use effective contraception during treatment with KEYTRUDA and for at least 4 months after the last dose of KEYTRUDA.
- **Nursing mothers**: It is unknown whether KEYTRUDA is secreted in human milk. Because many drugs are secreted in human milk, a decision should be made whether to discontinue breastfeeding or to discontinue KEYTRUDA, taking into account the benefit of breastfeeding for the child and the benefit of KEYTRUDA therapy for the woman.
- **Pediatric patients**: In cHL and PMBCL, the recommended dose of KEYTRUDA in pediatric patients is 2 mg/kg (up to a maximum of 200 mg), administered as an intravenous infusion over 30 minutes every 3 weeks.

  There is limited experience with KEYTRUDA in pediatric patients. In a study, 87 pediatric patients (36 children ages 9 months to less than 12 years and 51 adolescents ages 12 years to 18 years) with advanced melanoma, lymphoma, or PD-L1–positive advanced, relapsed, or refractory solid tumors were administered KEYTRUDA 2 mg/kg every 3 weeks. Patients received KEYTRUDA for a median of 3 doses (range: 1–26 doses), with 71 patients (82%) receiving KEYTRUDA for 2 doses or more. The concentrations of KEYTRUDA in pediatric patients were comparable to those observed in adult patients at the same dose regimen of 2 mg/kg every 3 weeks.

  The safety profile in these pediatric patients was similar to that seen in adults treated with KEYTRUDA. The most common adverse reactions (reported in at least 20% of pediatric patients) were pyrexia, vomiting, fatigue, constipation, abdominal pain and nausea.

  Efficacy for pediatric patients with cHL or PMBCL is extrapolated from the results in the respective adult populations
- **Geriatric patients**: No overall differences in safety or efficacy were reported between elderly patients (65 years and over) and younger patients (less than 65 years). No dose adjustment is necessary in this population.
- **Renal impairment**: No dose adjustment is needed for patients with mild or moderate renal impairment. KEYTRUDA has not been studied in patients with severe renal impairment.
- **Hepatic impairment**: No dose adjustment is needed for patients with mild hepatic impairment. KEYTRUDA has not been studied in patients with moderate or severe hepatic impairment.

CCDS: p12C

CCDS: p12D

CCDS: p8E; p12E; p13A,B

CCDS: p8E

CCDS: p8E

CCDS: p8E

For information about how to manage adverse events associated with KEYTRUDA in combination therapy, please see the labeling information for the appropriate treatment.

KEYTRUDA™
(pembrolizumab) Injection 100 mg

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

Guide your patients through treatment with KEYTRUDA™

CCDS: p6A

CCDS: p5D; p8E

Your patients may not be familiar with KEYTRUDA or what to expect throughout treatment. Here is a road map with a few discussion points that may be useful during conversations about the treatment plan.

1. DISCUSS

CCDS: p85C
ACS - Immunotherapy 2019: p1A,B; p2B

- KEYTRUDA is an immunotherapy that works with the body's immune system to help fight cancer.[1]

Villadolid, 2015: p573J; p574A,B

Talk with your patients about immunotherapy:

KEYTRUDA is an immunotherapy—not a chemotherapy. Side effects may be different from those you might have had with chemotherapy and may be treated differently.[2]

2. START

- KEYTRUDA offers 3 different dosing options: 200 mg Q3W, 400 mg Q6W, and 2 mg/kg Q3W, all administered as a 30-minute infusion.[a,b]
- Treatment with KEYTRUDA should continue until disease progression or unacceptable toxicity.

For additional information, please see pages 9–11.

CCDS: p5D

Talk with your patients about starting treatment with KEYTRUDA:

You will receive a 30-minute infusion of KEYTRUDA every 3 or 6 weeks for as long as KEYTRUDA is working and side effects are tolerable.[a]

3. MONITOR

- Immune-mediated adverse reactions may occur at any time throughout treatment.
- Monitor patients regularly and encourage them to immediately report any changes in their health. This may help keep problems from becoming more serious.[2,3]

For additional information, please see pages 14–19.

Talk with your patients about monitoring:

Contact your cancer care team immediately if you have any symptoms of side effects. The sooner side effects are reported, the sooner you can be treated.[2,3]

4. MANAGE

- Most of the common adverse events reported with KEYTRUDA in clinical trials were Grade 1 or 2. Immune-mediated adverse reactions were managed with interruptions or discontinuation of KEYTRUDA, administration of corticosteroids, and/or supportive care.

5. FOLLOW UP

- Adverse events can occur at any time during treatment and may occur later compared with other cancer therapies.[3] The time to onset of immune-mediated adverse reactions reported with KEYTRUDA ranged from 1 day to 22 months after the first dose.

CCDS: p9B; p14A

CCDS: p14B,C; p15A
Kannan, 2014: p316G,H

Talk with your patients about the side effects of KEYTRUDA:

Side effects may occur at any time. Side effects with KEYTRUDA in clinical trials have occurred as early as 1 day or as late as nearly 2 years after first infusion. KEYTRUDA may be given as long as it is working and side effects are tolerable.

CCDS: p6A; p14B,C; p15A

Villadolid, 2015: p574B
Kannan, 2014: p316A,F

CCDS: p9B
Villadolid, 2015: p574B
Kannan, 2014: p316B,D,F

CCDS: p9B

[a]Q6W dosing is only for monotherapy indications.
[b]2 mg/kg Q3W dosing is for pediatric patients with cHL or PMBCL.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

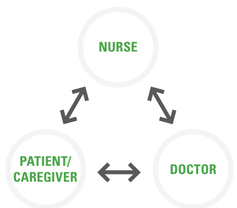
KEYTRUDA™ (pembrolizumab) Injection 100 mg

Monitoring for adverse events

Monitoring for adverse events is a collaborative effort

Communication is essential to managing treatment[4]

Appropriate management of adverse events may depend on timely identification and education of all those involved in the patient's care. Patients receiving KEYTRUDA™, and their health care providers, should be educated to recognize and report any signs and symptoms that may occur during treatment.



Regular communication between you and your patients, as well as within the entire cancer care team, can enhance the treatment experience.[3,4]

- Notify the rest of the cancer care team of any changes to your patient's health.[5]
- Expand your cancer care network to include specialists such as endocrinologists.[5]
- Inform patients and caregivers of potential side effects and ask them to immediately report any symptoms.[4,5]

Throughout treatment, remind your patients to tell health care professionals outside of their cancer care team that they are receiving KEYTRUDA. Ensure that they have your appropriate contact information on hand in case they need to see their primary care physician, consult with a pharmacist, or visit the emergency room.[5]

Talking with your patients about informing other health care professionals[5]:

- Throughout treatment with KEYTRUDA, you will speak with your nurse and see your oncologist regularly. You may also see a health care provider outside of your cancer care team. If you do see your primary care doctor, a pharmacist, or even an emergency room doctor or nurse, make sure to tell them you are being treated with immunotherapy, not chemotherapy.
- Ask your doctor or nurse for your care team's contact information. Share this contact information with any health care provider you may see.

Adverse events can occur during treatment with KEYTRUDA

Clinical trial experience across multiple studies

- The safety of KEYTRUDA was evaluated in 2,799 patients.
- The median treatment duration was 4.2 months (range: 1 day to 30.4 months), including 1,153 patients treated for ≥6 months and 600 patients treated for ≥1 year.
- 5% of patients discontinued KEYTRUDA for treatment-related adverse reactions.
- Treatment-related serious adverse events reported up to 90 days after the last dose occurred in 10% of patients receiving KEYTRUDA.
- Adverse events can occur at any time during treatment and may occur later compared with other cancer therapies. In clinical trials, adverse events occurred as late as 22 months after the first doses of KEYTRUDA.

Talking with your patients about reporting side effects:

- It is important to tell your cancer care team right away if you have a side effect that does not go away.[2,3]
- The sooner you report any side effects, the sooner you can be managed.[2,3]
- KEYTRUDA may be given as long as it is working and side effects are tolerable.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

Fecher: p736C

Kannan, 2014: p316C
Teply: p37A,B

Teply: p37A,B

CCDS: p13B; p14B,C; p15A

CCDS: p6A; p9B,C
Villadolid, 2015: p574B
Kannan, 2014: p316B

Fecher: p736A,D

Fecher: p736A-D

Fecher: p736A
Teply: p32A

Fecher: p736B

Gangadhar: p92A; p97A; p98A

Luke, 2015: p3485A

Luke, 2015: p3485A
Patel, 2015: p848A-C

CCDS: p9B

CCDS: p13C; p14A

CCDS: p11B

Kannan, 2014: p316D,E
Gangadhar, 2014: p94E
DeVita, 2008: p409A; p410A; p415C; p449A

Villadolid, 2015: p574B
Luke, 2015: p3484A; p3485A
DeVita, 2008: p415B,C

Anti–PD-1 therapy can cause adverse events that involve the immune system[6]

Adverse reactions with KEYTRUDA™ may be different from those with chemotherapy[7]

- Immunotherapies reactivate the body's immune responses. Adverse events may be caused by the activation of potentially self-reactive T cells that could also affect normal healthy cells.[7,8]

In clinical trials, most immune-mediated adverse reactions with KEYTRUDA were reversible and managed with interruptions of KEYTRUDA, administration of corticosteroids, and/or supportive care.

Adverse reaction	KEYTRUDA 2 mg/kg every 3 weeks or 10 mg/kg every 2 or 3 weeks (N=2,799)				
	All grades (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)
Hypothyroidism[a]	8.5	6.2	0.1	0	0
Hyperthyroidism	3.4	0.8	0.1	0	0
Pneumonitis[b]	3.4	1.3	0.9	0.3	0.1
Colitis	1.7	0.4	1.1	<0.1	0
Adrenal insufficiency	0.8	0.3	0.3	<0.1	0
Hepatitis	0.7	0.1	0.4	<0.1	0
Hypophysitis	0.6	0.2	0.3	<0.1	0
Nephritis[c]	0.3	0.1	0.1	<0.1	0
Type 1 diabetes mellitus	0.2	<0.1	0.1	0.1	0

[a]In individual studies of patients with HNSCC treated with KEYTRUDA as monotherapy (n=909), the incidence of hypothyroidism was 16.1% (all grades) with 0.3% Grade 3. In patients with HNSCC treated with KEYTRUDA in combination with platinum and 5-FU chemotherapy (n=276), the incidence of hypothyroidism was 15.2%, all of which were Grade 1 or 2. In patients with cHL (n=241), the incidence of hypothyroidism was 14.1% (all grades), with 0.4% Grade 3.

[b]In individual studies of patients with NSCLC treated with KEYTRUDA as monotherapy (total n=2,022), the incidence of pneumonitis (all grades) ranged from 3.8% to 8.3%.

[c]In patients with nonsquamous NSCLC treated with KEYTRUDA 200 mg in combination with pemetrexed and platinum chemotherapy (n=405), the incidence of nephritis was 1.7% (all grades), with 1.0% Grade 3 and 0.5% Grade 4.

The following additional clinically significant, immune-mediated adverse reactions were reported in less than 1% of patients treated with KEYTRUDA in KEYNOTE-001, KEYNOTE-002, KEYNOTE-006, and KEYNOTE-010: uveitis, myositis, Guillain-Barré syndrome, pancreatitis, encephalitis, sarcoidosis, and myasthenic syndrome/myasthenia gravis (including exacerbation). The following was reported in other clinical studies with KEYTRUDA or in post-marketing use: myocarditis.

- Certain types of adverse events (such as pneumonitis and diarrhea) that occur with traditional anti-tumor therapies also occur with immunotherapies.[3,6,9]
- The underlying cause of the adverse event may be different. For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes.[2,7,9]
- See **pages 20–29** for more information about managing select immune-mediated adverse reactions.

Most common adverse events reported with KEYTRUDA were Grade 1 or 2

Unresectable or metastatic melanoma: Adverse events occurring in ≥10% of patients treated with KEYTRUDA and at a higher incidence than in the ipilimumab arm in KEYNOTE-006[d]

Adverse event	KEYTRUDA 10 mg/kg every 2 or 3 weeks (n=555)		Ipilimumab 3 mg/kg every 3 weeks (n=256)	
	All grades (%)	Grade 3[e] (%)	All grades (%)	Grade 3[e] (%)
Musculoskeletal and connective tissue disorders				
Arthralgia	18	0	10	1
Back pain	12	1	7	1
Respiratory, thoracic and mediastinal disorders				
Cough	17	0	7	0
Skin and subcutaneous tissue disorders				
Vitiligo	11	0	2	0

[d]Between-arm difference of ≥5% (all grades) or ≥2% (Grade 3).

[e]Of these ≥10% adverse events, none was reported as Grade 4.

- The most common adverse events (reported in ≥15% of patients) were arthralgia and cough.

Unresectable or metastatic melanoma: Adverse events occurring in ≥10% of patients with melanoma treated with KEYTRUDA and at a higher incidence than in the chemotherapy arm in KEYNOTE-002[f]

Adverse event	KEYTRUDA 2 mg/kg every 3 weeks (n=178)		Chemotherapy (n=171)	
	All grades (%)	Grades 3–4[g] (%)	All grades (%)	Grades 3–4[g] (%)
Gastrointestinal disorders				
Abdominal pain	13	2	8	1
Skin and subcutaneous tissue disorders				
Pruritus	25	0	8	0
Rash	13	0	8	0
Metabolism and nutrition disorders				
Hyponatremia	11	3	5	1
Musculoskeletal and connective tissue disorders				
Arthralgia	15	1	10	1

[f]Between-arm difference of ≥5% (all grades) or ≥2% (Grades 3–4).

[g]Of these ≥10% adverse events, none was reported as Grade 4 in patients receiving KEYTRUDA at 2 mg/kg. Hyponatremia was reported as Grade 4 in one patient receiving chemotherapy.

- The most common adverse event (reported in ≥20% of patients) was pruritus.
- Overall, the safety profile was similar across all doses and between patients previously treated with ipilimumab and patients naïve to treatment with ipilimumab.

Resected melanoma: Among the 1,019 patients with resected melanoma enrolled in KEYNOTE-054, the adverse reactions were generally similar to those occurring in patients with unresectable or metastatic melanoma or NSCLC.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

CCDS: p14A

CCDS: p15B

CCDS: p16A

CCDS: p15B: p16A

CCDS: p16B

CCDS: p17A

CCDS: p16C

CCDS: p17B

Adverse events reported with KEYTRUDA™

NSCLC as combination therapy: Adverse events occurring in ≥20% of patients receiving KEYTRUDA with pemetrexed and platinum chemotherapy and at a higher incidence than in patients receiving placebo with pemetrexed and platinum chemotherapy in KEYNOTE 189[a]

Adverse event	KEYTRUDA + pemetrexed + platinum chemotherapy (n=405)		Placebo + pemetrexed + platinum chemotherapy (n=202)	
	All grades[b] (%)	Grades 3–4 (%)	All grades (%)	Grades 3–4 (%)
General disorders and administration site conditions				
Fatigue	41	6	38	2.5
Asthenia	20	6	24	3.5
Gastrointestinal disorders				
Diarrhea	31	5	21	3.0
Blood and lymphatic system disorders				
Neutropenia	27	16	24	12
Skin and subcutaneous tissue disorders				
Rash	20	1.7	11	1.5

[a]Between-arm difference of ≥5% (all grades) or ≥2% (Grade 3–4).
[b]Graded per NCI-CTCAE v4.03.

- Adverse events occurring in previously untreated patients with NSCLC receiving KEYTRUDA in combination with carboplatin and either paclitaxel or nab-paclitaxel in KEYNOTE-407 were generally similar to those occurring in patients in KEYNOTE-189 with the exception of alopecia (46%) and arthralgia (21%).

NCI-CTCAE = National Cancer Institute-Common Terminology Criteria for Adverse Events.

NSCLC as monotherapy: Adverse events occurring in ≥10% of NSCLC patients treated with KEYTRUDA and at a higher incidence than in the chemotherapy arm in KEYNOTE-042[c]

Adverse event	KEYTRUDA 200 mg every 3 weeks (n=636)		Chemotherapy (n=615)	
	All grades[d] (%)	Grades 3–5 (%)	All grades (%)	Grades 3–5 (%)
Respiratory, thoracic, and mediastinal disorders				
Dyspnea	17	2.0	11	0.8
Cough	16	0.2	11	0.3
Endocrine disorders				
Hypothyroidism	12	0.2	1.5	0

[c]Between-arm difference of ≥5% (all grades) or ≥2% (Grades 3–5).
[d]Graded per NCI-CTCAE v4.03.

- The most common adverse events (reported in at least 15% of patients) were dyspnea and cough.
- Adverse events occurring in previously untreated patients with NSCLC receiving KEYTRUDA in KEYNOTE-024 and previously treated patients in KEYNOTE-010 were generally similar to those occurring in patients in KEYNOTE-042.

Other cancers

CCDS: p18A

CCDS: p18B

CCDS: p18C

CCDS: p18D

CCDS: p18E

Monotherapy

Adverse events occurring in patients with SCLC, HNSCC, cHL, PMBCL, urothelial carcinoma, gastric cancer, esophageal cancer, MSI-H cancer, HCC, or cervical cancer were generally similar to those occurring in patients with melanoma or NSCLC.

Combination therapy

In patients with HNSCC receiving KEYTRUDA plus chemotherapy (platinum and 5-FU), adverse reactions occurring at a greater severity (Grades 3–4) and at a higher incidence (≥2% difference) compared to cetuximab plus chemotherapy (platinum and 5-FU) were: fatigue (7% vs 4.9%), mucosal inflammation (10% vs 5%), and stomatitis (8% vs 3.5%).

Renal cell carcinoma

Combination Therapy With Axitinib
The most common adverse reactions that occurred in at least 20% of previously untreated patients with RCC receiving KEYTRUDA and axitinib in KEYNOTE-426 were diarrhea, hypertension, fatigue, hypothyroidism, decreased appetite, palmar-plantar erythrodysaesthesia syndrome, nausea, ALT increased, AST increased, dysphonia, cough, and constipation.

In KEYNOTE-426, higher than expected incidence of Grades 3 and 4 ALT increased (20%) and AST increased (13%) was observed in previously untreated patients with RCC receiving KEYTRUDA in combination with axitinib. The median time to onset of ALT increased was 2.3 months (range: 7 days to 19.8 months). In patients with ALT ≥3 times ULN (Grades 2–4, n=116), ALT resolved to Grades 0–1 in 94%. Fifty-nine percent of the patients with increased ALT received systemic corticosteroids. Of the patients who recovered, 92 (84%) were rechallenged with either KEYTRUDA (3%) or axitinib (31%) monotherapy or with both (50%). Of these patients, 55% had no recurrence of ALT >3 times ULN, and of those patients with recurrence of ALT >3 times ULN, all recovered. There were no Grade 5 hepatic events.

Postmarketing experience

The following adverse reactions have been identified during post-approval use of KEYTRUDA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Musculoskeletal and connective tissue disorders: arthritis
Eye disorders: Vogt-Koyanagi-Harada syndrome
Immune system disorders: hemophagocytic lymphohistiocytosis

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

Managing adverse events associated with KEYTRUDA™

Immune-mediated pneumonitis

Monitor

Monitor for signs and symptoms of pneumonitis.

If pneumonitis is suspected, evaluate with radiographic imaging and exclude other causes.

- **Incidence (all grades):** 3.4% of 2,799 patients with unresectable or metastatic melanoma or advanced NSCLC receiving KEYTRUDA
  - Grade 5 pneumonitis was reported in 0.1% of patients.
- **Discontinuation rate:** 1.3% of 2,799 patients
- **Median time to onset:** 3.3 months (range: 2 days to 19.3 months)
- **Median duration:** 1.5 months (range: 10 days to 17.2+ months)

Ask patients to immediately report:

- Shortness of breath
- Chest pain
- Cough

Evaluate[10]

- **Grade 2:** Symptomatic; medical intervention indicated; limiting instrumental ADL[a]
- **Grade 3:** Severe symptoms; limiting self-care ADL[b]; oxygen indicated
- **Grade 4:** Life-threatening respiratory compromise; urgent intervention indicated (eg, tracheotomy or intubation)

Manage

- **Grade 2:** Withhold KEYTRUDA; administer corticosteroids
- **Grade 3 or 4: Permanently discontinue KEYTRUDA**
- **Also permanently discontinue KEYTRUDA:**
  - If corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day within 12 weeks after last dose
  - If treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA

[a]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[10]
[b]Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not being bedridden.[10]

ADL = activities of daily living.

KEY: Green: Continue usage of KEYTRUDA with monitoring.
Yellow: Withhold KEYTRUDA and administer corticosteroids.
Red: Discontinue KEYTRUDA.

Immune-mediated colitis

Monitor

Monitor for signs and symptoms of colitis and exclude other causes.

- Incidence (all grades): 1.7% of 2,799 patients with melanoma or NSCLC receiving KEYTRUDA
- Discontinuation rate: 0.5% of 2,799 patients
- Median time to onset: 3.5 months (range: 10 days to 16.2 months)
- Median duration: 1.3 months (range: 1 day to 8.7+ months)

Ask patients to immediately report:

- Diarrhea or more bowel movements than usual
- Stools that are black, tarry, sticky, or have blood or mucus
- Severe stomach pain or tenderness

Evaluate[10]

- **Grade 2:** Abdominal pain; mucus or blood in stool
- **Grade 3:** Severe abdominal pain; peritoneal signs
- **Grade 4:** Life-threatening consequences; urgent intervention indicated

Manage

- **Grade 2 or 3:** Withhold KEYTRUDA; administer corticosteroids
- **Grade 4: Permanently discontinue KEYTRUDA**
- **Also permanently discontinue KEYTRUDA:**
  - If corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day within 12 weeks after last dose of KEYTRUDA
  - If treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

CCDS: p9D; p14A,C

CCPPI: p3A,B

CTCAE, v5.0: p137A

CCDS: p6B; p7E; p9D

CTCAE, v5.0: p2A

CCDS: p9E; p13C; p14A,C

CCPPI: p3A,C

CTCAE, v5.0: p26A

CCDS: p6C; p7E; p9E

Managing adverse events associated with KEYTRUDA™ (*continued*)

CCDS: p9F; p10A; p13C; p14A,C

CCPPI: p3A,D

CTCAE, v5.0: p84B; p85A
CCDS: p6F; p7A

CCDS: p6F; p7A,E; p9C,F; p10A

Immune-mediated hepatitis (for non-HCC patients)

Monitor

Monitor patients for changes in liver function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and symptoms of hepatitis and exclude other causes.

- **Incidence (all grades):** 0.7% of 2,799 patients with unresectable or metastatic melanoma or advanced NSCLC receiving KEYTRUDA
- **Discontinuation rate:** 0.2% of 2,799 patients
- **Median time to onset:** 1.3 months (range: 8 days to 21.4 months)
- **Median duration:** 1.8 months (range: 8 days to 20.9+ months)

Ask patients to immediately report:

- Nausea or vomiting
- Feeling less hungry
- Pain on the right side of stomach
- Yellowing of skin
- Yellowing of the whites of eyes
- Dark urine
- Bleeding or bruising more easily than normal

Evaluate[10]

- **Grade 2:** ALT and/or AST increased >3 to 5 times ULN; blood bilirubin increased >1.5 to 3 times ULN.
- **Grade 3:** ALT and/or AST increased >5 to 20 times ULN; blood bilirubin increased >3 to 10 times ULN.
- **Grade 4:** ALT and/or AST increased >20 times ULN; blood bilirubin increased >10 times ULN.

Manage

Administer corticosteroids[a] and, based on severity of liver enzyme elevations, withhold or permanently discontinue KEYTRUDA.

- Withhold KEYTRUDA for AST or ALT >3 to 5 times ULN or total bilirubin >1.5 to 3 times ULN.
- Upon improvement to **Grade 1** or less, initiate corticosteroid taper and continue to taper over at least 1 month.
- Restart KEYTRUDA if the adverse reaction remains at Grade 1 or less following corticosteroid taper.
- **Permanently discontinue KEYTRUDA:**
  - For immune-mediated hepatitis in patients with:
    - AST or ALT >5 times ULN or total bilirubin >3 times ULN
    - For patients with liver metastasis who begin treatment with moderate (Grade 2) elevation of AST or ALT, if AST or ALT increases ≥50% relative to baseline and lasts ≥1 week
  - If corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day within 12 weeks
  - If a treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA
  - If another episode of any severe toxicity occurs

KEY: Green: Continue usage of KEYTRUDA with monitoring.
Yellow: Withhold KEYTRUDA and administer corticosteroids.
Red: Discontinue KEYTRUDA.

Immune-mediated hepatitis (for HCC patients)

Monitor

Monitor patients for changes in liver function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and symptoms of hepatitis and exclude other causes.

- **Incidence (all grades):** 0.7% of 2,799 patients with melanoma or NSCLC receiving KEYTRUDA
- **Discontinuation rate:** 0.2% of 2,799 patients
- **Median time to onset:** 1.3 months (range: 8 days to 21.4 months)
- **Median duration:** 1.8 months (range: 8 days to 20.9+ months)

Ask patients to immediately report:

- Nausea or vomiting
- Feeling less hungry
- Pain on the right side of stomach
- Yellowing of skin
- Yellowing of the whites of eyes
- Dark urine
- Bleeding or bruising more easily than normal

Evaluate[10]

- **Grade 2:** ALT and/or AST increased >3 to 5 times ULN; blood bilirubin increased >1.5 to 3 times ULN.
- **Grade 3:** ALT and/or AST increased >5 to 20 times ULN; blood bilirubin increased >3 to 10 times ULN.
- **Grade 4:** ALT and/or AST increased >20 times ULN; blood bilirubin increased >10 times ULN.

Manage

Administer corticosteroids[a] and, based on severity of liver enzyme elevations, withhold or permanently discontinue KEYTRUDA.

- Withhold KEYTRUDA for AST or ALT with baseline <2 times ULN and increases to ≥5 times ULN; AST or ALT with baseline ≥2 times ULN and increases to >3 times baseline or AST or ALT >500 U/L regardless of baseline levels.
- Withhold KEYTRUDA for total bilirubin with baseline levels <1.5 mg/dL and increases to >2 mg/dL; total bilirubin with baseline levels ≥1.5 mg/dL and increases to ≥2 times baseline: or total bilirubin >3.0 mg/dL regardless of baseline levels
- Upon improvement to **Grade 1** or less, initiate corticosteroid taper and continue to taper over at least 1 month.
- Restart KEYTRUDA if the adverse reaction remains at **Grade 1** or less following corticosteroid taper.
- **Permanently discontinue KEYTRUDA:**
  - For patients with:
    - ALT >20 times ULN
    - Child Pugh score ≥9 points
    - Gastrointestinal bleeding suggestive of hypertension, ascites, or encephalopathy
  - If corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day within 12 weeks
  - If a treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA
  - If another episode of any severe toxicity occurs

[a]Refer to the Prescribing Information for recommended initial corticosteroid dosing.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

CCDS: p9F; p10A; p14A,C

CCPPI: p3A,D

CTCAE, v5.0: p84B,D; p85A
CCDS: p7B

CCDS: p7B,C,E; p9C,F; p10A

Managing adverse events associated with KEYTRUDA™ (*continued*)

CCDS: p10C; p13C; p14A,B

CCPPI: p3A; p4A,B

CTCAE, v5.0: p16A

CCDS: p7E; p10C,E,F

Immune-mediated hypophysitis

Monitor

Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and secondary adrenal insufficiency) and exclude other causes.

- **Incidence (all grades):** 0.6% of 2,799 patients with melanoma or NSCLC receiving KEYTRUDA
- **Discontinuation rate:** 0.1% of 2,799 patients
- **Median time to onset:** 3.7 months (range: 1 day to 11.9 months)
- **Median duration:** 4.7 months (range: 8+ days to 12.7+ months)

Ask patients to immediately report:

- Headaches that will not go away or unusual headache
- Changes in eyesight

Evaluate[10]

- **Grade 2:** Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental ADL[a]
- **Grade 3:** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; limiting self-care ADL[b]
- **Grade 4:** Life-threatening consequences; urgent intervention indicated

Manage

- **Grade 2:** Withhold KEYTRUDA and administer corticosteroids to treat secondary adrenal insufficiency and other hormone replacement therapy as clinically indicated.
- **Grade 3 or 4:** Withhold or discontinue KEYTRUDA and administer corticosteroids to treat secondary adrenal insufficiency and other hormone replacement as clinically indicated.
  - For patients whose endocrinopathy improves to **Grade 2** or lower and is controlled with hormone replacement, if indicated, continuation of KEYTRUDA may be considered after corticosteroid taper, if needed. Otherwise, treatment should be discontinued.
- **Also permanently discontinue KEYTRUDA:**
  - If a treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA
  - If another episode of any severe toxicity occurs

KEY: Green: Continue usage of KEYTRUDA with monitoring.
Yellow: Withhold KEYTRUDA and administer corticosteroids.
Red: Discontinue KEYTRUDA.

Immune-mediated hypothyroidism

Monitor

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for signs and symptoms of thyroid disorders.

- **Incidence (all grades):** 8.5% of 2,799 patients with unresectable or metastatic melanoma or advanced NSCLC receiving KEYTRUDA
- **Discontinuation rate:** <0.1% of 2,799 patients
- **Median time to onset:** 3.5 months (range: 1 day to 18.9 months)
- **Median duration:** Not reached (range: 2 days to 27.7+ months)

Ask patients to immediately report[11]:

- Dry skin
- Cold sensitivity
- Feeling tired
- Muscle cramps
- Voice changes
- Constipation

Evaluate[10]

- **Grade 2:** Symptomatic; thyroid replacement therapy indicated; instrumental ADL limited[a]
- **Grade 3:** Severe symptoms; limiting self-care ADL[b]; hospitalization indicated
- **Grade 4:** Life-threatening consequences; urgent intervention indicated

Manage

- Withhold KEYTRUDA for patients with severe or life-threatening (**Grade 3 or 4**) endocrinopathies.
- For patients with severe (**Grade 3**) or life-threatening (**Grade 4**) endocrinopathy that improves to **Grade 2** or lower and is controlled with hormone replacement, continuation of KEYTRUDA may be considered. Otherwise, treatment should be discontinued.
- Hypothyroidism may be managed with replacement therapy without treatment interruption and without corticosteroids.
- **Also permanently discontinue KEYTRUDA:**
  - If a treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA
  - If another episode of any severe toxicity occurs

[a]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[10]
[b]Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not being bedridden.[10]

CCDS: p10E; 13C; p14A,B
Garber, 2012: p1207A

CTCAE, v5.0: p16B

CCDS: p6E; p7E; p9C; p10E

CTCAE, v5.0: p2A

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

Managing adverse events associated with KEYTRUDA™ (*continued*)

CCDS: p10E; p13C; p14A,B

CCPPI: p3A,C,E; p4A,B
Hamnvik: p1573A

CTCAE, v5.0: p15A

CCDS: p6E; p7E; p9C; p10E

CTCAE, v5.0: p2A

Immune-mediated hyperthyroidism

Monitor

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for signs and symptoms of thyroid disorders.

- **Incidence (all grades):** 3.4% of 2,799 patients with melanoma or NSCLC receiving KEYTRUDA
- **Discontinuation rate:** <0.1% of 2,799 patients
- **Median time to onset:** 1.4 months (range: 1 day to 21.9 months)
- **Median duration:** 2.1 months (range: 3 days to 15.0+ months)

Ask patients to immediately report[12]:

- Rapid heartbeat
- Weight loss
- Heat intolerance
- Frequent bowel movements
- Muscle weakness
- Trouble sleeping
- Irritability
- Fever

Evaluate[10]

- **Grade 2:** Symptomatic; thyroid suppression therapy indicated; limiting instrumental ADL[a]
- **Grade 3:** Severe symptoms; limiting self-care ADL[b]; hospitalization indicated
- **Grade 4:** Life-threatening consequences; urgent intervention indicated

Manage

- **Grade 2:** Manage symptomatically.
- **Grade 3 or 4:** Withhold or discontinue KEYTRUDA until adverse reactions recover to **Grades 0–2**.
  - For patients whose endocrinopathy improves to **Grade 2** or lower and is controlled with hormone replacement, if indicated, continuation of KEYTRUDA may be considered. Otherwise, treatment should be discontinued.
- **Also permanently discontinue KEYTRUDA:**
  - If a treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA
  - If another episode of any severe toxicity occurs

[a]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[10]
[b]Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not being bedridden.[10]

KEY: Green: Continue usage of KEYTRUDA with monitoring.
Yellow: Withhold KEYTRUDA and administer corticosteroids.
Red: Discontinue KEYTRUDA.

Immune-mediated nephritis

Monitor

Monitor patients for changes in renal function and exclude other causes.

- **Incidence (all grades):** 0.3% of 2,799 patients with melanoma or NSCLC receiving KEYTRUDA
- **Discontinuation rate:** 0.1% of 2,799 patients
- **Median time to onset:** 5.1 months (range: 12 days to 12.8 months)
- **Median duration:** 3.3 months (range: 12 days to 8.9+ months)

Ask patients to immediately report:

- Change in amount or color of urine

Evaluate[10]

- **Grade 2:** Creatinine increased >1.5 to 3 times baseline; >1.5 to 3 times ULN
- **Grade 3:** Creatinine increased >3 times baseline; >3 to 6 times ULN
- **Grade 4:** Creatinine increased >6 times ULN

Manage

- **Grade 2:** Withhold KEYTRUDA and administer corticosteroids. Refer to prescribing information for recommended corticosteroid initial dosing.
  - Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month.
  - Restart KEYTRUDA if the adverse reaction remains at **Grade 1** or less following corticosteroid taper.
- **Grade 3 or 4:** Permanently discontinue KEYTRUDA; administer corticosteroids. Refer to prescribing information for recommended corticosteroid initial dosing.
- **Also permanently discontinue KEYTRUDA:**
  - If corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day within 12 weeks
  - If treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA
  - If another episode of any severe toxicity occurs

CCDS: p10B; p13C; 14A; p15A

CCPPI: p3E

CTCAE, v5.0: p86A

CCDS: p6D; p7E; p9C; p10B

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

Managing adverse events associated with KEYTRUDA™ (*continued*)

CCDS: p10D; p13C; p14A

CCPPI: p4A

CTCAE, v5.0: p92A

CCDS: p6E; p7E; p10D

Immune-mediated type 1 diabetes mellitus

Monitor

Monitor patients for hyperglycemia (including diabetic ketoacidosis) or other signs and symptoms of diabetes and exclude other causes.

- **Incidence (all grades):** 0.2% of 2,799 patients with unresectable or metastatic melanoma or advanced NSCLC receiving KEYTRUDA
- **Discontinuation rate:** 0.1% of 2,799 patients

Ask patients to immediately report:

- Feeling more hungry or thirsty
- Needing to urinate more often
- Weight loss

Evaluate[10]

- **Grade 2:** Change in daily management from baseline for a diabetic; oral antiglycemic agent initiated; workup for diabetes
- **Grade 3:** Insulin therapy initiated; hospitalization indicated
- **Grade 4:** Life-threatening consequences; urgent intervention indicated

Manage

- Type 1 diabetes mellitus, including diabetic ketoacidosis, has been reported in patients receiving KEYTRUDA.
- Administer insulin for type 1 diabetes and withhold KEYTRUDA in cases of severe hyperglycemia until metabolic control is achieved.
- **Permanently discontinue KEYTRUDA** for life-threatening (**Grade 4**) toxicity except for endocrinopathies that improve to **Grade 2** or lower and are controlled with replacement hormones.
- **Also permanently discontinue KEYTRUDA:**
  - If treatment-related toxicity does not resolve to **Grades 0–1** within 12 weeks after last dose of KEYTRUDA
  - If another episode of any severe toxicity occurs

KEY: Green: Continue usage of KEYTRUDA with monitoring.
Yellow: Withhold KEYTRUDA and administer corticosteroids.
Red: Discontinue KEYTRUDA.

Immune-mediated severe skin reactions, SJS, and TEN

Monitor

- Monitor patients for suspected severe skin reactions and exclude other causes. Cases of SJS, some with fatal outcome, have been reported in patients treated with KEYTRUDA.
- SJS is a disorder characterized by <10% total body skin area (BSA) separation of dermis. The syndrome is thought to be a hypersensitivity complex affecting the skin and the mucous membranes.[10]
- TEN is a disorder characterized by >30% total BSA separation of dermis. The syndrome is thought to be a hypersensitivity complex affecting the skin and the mucous membranes.[10]

Ask patients to immediately report:

- Rash
- Itching
- Skin blistering, peeling, or sores
- Ulcers in mouth or in lining of nose, throat, or genital area

Evaluate[10]

- **Grade 3:** Skin sloughing covering <10% BSA with associated signs (eg, erythema, purpura, epidermal detachment, and mucous membrane detachment)
- **Grade 4:** Skin sloughing covering 10%–30% BSA with associated signs (eg, erythema, purpura, epidermal detachment, and mucous membrane detachment)

Manage

Immune-mediated severe skin reactions:

- Based on the severity of the adverse reaction, withhold or permanently discontinue KEYTRUDA and administer corticosteroids.

SJS and TEN:

- Withhold KEYTRUDA for suspected SJS or TEN (**Grade 3**) and refer the patient for specialized care for assessment and treatment.
- **Permanently discontinue KEYTRUDA** if SJS or TEN is confirmed (**Grade 4**).

[a]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[10]
[b]Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not being bedridden.[10]
SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis.

CCDS: p10F; p11A
CTCAE, v5.0: p148A

CCPPI: p4B

CTCAE, v5.0: p148A

CCDS: p10F; p11A

CTCAE, v5.0: p2A

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

KEYTRUDA™ (pembrolizumab) Injection 100 mg

Patient care plan

ASCO - The Importance of Follow-Up Care: p1A,B

ASCO - The Importance of Follow-Up Care: p1B,C; p2A,B,D; p3A,B

ASCO - Healthy Living After Cancer: p1A,B; p2C,D

ASCO - The Importance of Follow-Up Care: p2A-D

ASCO - Healthy Living After Cancer: p1B; p2C,D

ASCO - Healthy Living After Cancer: p2C

ASCO - The Importance of Follow-Up Care: p1A,B

Once a treatment decision is made, talk with your patients about developing a survivorship plan. A personalized Survivorship Care Plan summarizes critical information on the patient journey thus far, as well as information needed for adequate long-term care.[13]

Implemented by the cancer care team, a Survivorship Care Plan should include[13,14]:

- Cancer type/stage, current treatment, and its potential side effects
  - Diagnostic tests and results
  - Prior treatment (including chemotherapy, radiation, targeted therapies, etc), dates received, dosing regimens, treatment response, and toxicities
  - Clinical trial participation
  - Psychosocial, nutritional, and supportive interventions
- Recommended follow-up schedule of screenings and other tests
- Preventative tips for well-being, including diet, exercise, and mental health
- Employment rights and health insurance support
- Psychological support, referrals to specialists and support groups, and a list of reliable resources for information

Benefits of implementing a personalized Survivorship Care Plan[13]:

- Introducing the plan may provide the patient with guidance.
- Patients may be motivated to become more active in their treatment.
- When shared with the entire cancer care team, including primary care physicians, it may help guide subsequent health care treatment.

To learn more about resources available for you and your patients, visit keytrudahcp.com.

Website address should be revised at the local level.

Notes

A quick guide to KEYTRUDA™

Demonstrated efficacy in 14 distinct tumor types across 26 KEYNOTE trials (as of December 2019)

Guide your patients through treatment with KEYTRUDA

Start	Monitor	Manage
		
Treat patients with KEYTRUDA • For pediatric patients: 2 mg/kg (up to 200 mg) every 3 weeks[a] • For adult patients: 200 mg every 3 weeks or 400 mg every 6 weeks[b]	Monitor your patients early and often and encourage them to promptly report any side effects.	Manage adverse events in accordance with recommended dose modifications, based on grade.

[a]2 mg/kg Q3W dosing is for pediatric patients with cHL or PMBCL.
[b]Q6W dosing is only for monotherapy indications.

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MSD

KEYTRUDA™ (pembrolizumab) Injection 100 mg

CCDS: p19A; p23A; p25D; p27C; p29B; p33C; p37B; p39B; p42C; p46B; p47C; p49B; p55C; p57B; p58C; p60C; p61C; p63C; p66C; p67F; p69A; p72B; p73C; p75B; p76B; p77C

CCDS: p5B-D; p6A; p9B,C

Website address should be revised at the local level.