SELECTED SAFETY INFORMATION

- Immune-mediated adverse reactions, which may be severe or fatal, can occur with KEYTRUDA, including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis, severe skin reactions, solid organ transplant rejection, and complications of allogeneic HSCT. Based on the severity of the adverse reaction, KEYTRUDA should be withheld or discontinued and corticosteroids administered if appropriate. For more information regarding immune-mediated adverse reactions, please read the additional Selected Safety Information on pages 12 to 19.

HSCT = hematopoietic stem cell transplantation

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.
Melanoma
- KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma.
- KEYTRUDA is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.

Merkel Cell Carcinoma
- KEYTRUDA is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC). This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Non–Small Cell Lung Cancer
- KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
- KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein–bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
- KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [tumor proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.
- KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.

Small Cell Lung Cancer
- KEYTRUDA is indicated for the treatment of patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy and at least 1 other prior line of therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Head and Neck Cancer
- KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC) whose tumors express PD-L1 (combined positive score [CPS] ≥1) as determined by an FDA-approved test. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Cutaneous Squamous Cell Carcinoma
- KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma (cSCC) that is not curable by surgery or radiation.

EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1.
KEYTRUDA is approved for a range of patients

Indications (continued)

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. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Primary Mediastinal Large B-Cell Lymphoma
• KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after 2 or more prior lines of therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. KEYTRUDA is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

Urothelial Carcinoma
• KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (mUC) who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

• KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with 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) and who have not received prior BCG therapy.

Microsatellite Instability-High Cancers
• KEYTRUDA is indicated for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer.

• KEYTRUDA is recommended for treatment of patients with MSI-H or dMMR colorectal cancer.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide is also available.
KEYTRUDA is approved for a range of patients

Indications (continued)

Gastric Cancer

• KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDAt-approved 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. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Esophageal Cancer

• KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic esophageal adenocarcinoma whose tumors express PD-L1 (CPS ≥10) as determined by an FDAt-approved test, with disease progression after one or more prior lines of systemic therapy.

Cervical Cancer

• KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥10) as determined by an FDAt-approved test. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Hepatocellular Carcinoma

• KEYTRUDA is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Renal Cell Carcinoma

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

HER2 = human epidermal growth factor receptor 2.
KEYTRUDA binds to the PD-1 receptor, blocking both immune-suppressing ligands, PD-L1 and PD-L2, from interacting with PD-1 to help restore 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-L1 = programmed death ligand 1; PD-L2 = programmed death ligand 2.

TWO DOSING OPTIONS FOR KEYTRUDA

Choose an appropriate option for your patients

Adult patients: 300 mg
Pediatric patients (with cHL, PMBCL, MSI-H cancer, or MCC): 2 mg/kg (weight-based dosing, up to a maximum of 200 mg)

Administered as an intravenous infusion over 30 minutes

Every 6 Weeks

Adult patients: 400 mg

Pediatric patients (with cHL, PMBCL, MSI-H cancer, or MCC): 2 mg/kg (weight-based dosing, up to a maximum of 200 mg)

Administered as an intravenous infusion over 30 minutes

Every 6 Weeks

The 400-mg Q6W dosing regimen is approved under accelerated approval based on pharmacokinetic data, the relationship of exposure to efficacy, and the relationship of exposure to safety. Continued approval for this dosing may be contingent upon verification and description of clinical benefit in the confirmatory trials.

- For NSCLC, SCLC, HNSCC, cHL (adult and pediatric), PMBCL (adult and pediatric), locally advanced or metastatic urothelial carcinoma, MSI-H cancer (adult and pediatric), MSI-H/dMMR CRC, gastric cancer, esophageal cancer, cervical cancer, HCC, MCC (adult and pediatric), or cSCC: Treatment with KEYTRUDA should continue until disease progression, unacceptable toxicity, or up to 24 months.
- For unresectable or metastatic melanoma: Treatment should continue until disease progression or unacceptable toxicity.
- For adjuvant treatment of melanoma: Treatment should continue until disease recurrence, unacceptable toxicity, or for up to 12 months.
- For RCC: Treatment with KEYTRUDA + axitinib (5 mg orally bid) should continue until disease progression or unacceptable toxicity, or for KEYTRUDA, up to 24 months. When axitinib is used in combination with KEYTRUDA, dose escalation of axitinib above the initial 5-mg dose may be considered at intervals of 6 weeks or longer. Refer to the Prescribing Information for axitinib for recommended dosing information, as appropriate.
- For high-risk, BCG-unresponsive NMIBC: Treatment should continue until persistent or recurrent high-risk NMIBC, disease progression, unacceptable toxicity, or up to 24 months.

Q6W = every 6 weeks; bid = twice daily.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.
Use of KEYTRUDA in SPECIFIC POPULATIONS

PREGNANCY: Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose.

LACTATION: Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the final dose.

PEDIATRIC USE: There is limited experience in pediatric patients. In a trial, 40 pediatric patients (16 children aged 2 years to less than 12 years and 24 adolescents aged 12 years to 18 years) with various cancers, including unapproved usages, were administered KEYTRUDA 2 mg/kg every 3 weeks. Patients received KEYTRUDA for a median of 3 doses (range 1–17 doses), with 34 patients (85%) receiving 2 doses or more. The safety profile in these pediatric patients was similar to that seen in adults; adverse reactions that occurred at a higher rate (≥15% difference) in pediatric patients when compared to adults <65 years of age were fatigue (45%), vomiting (38%), abdominal pain (28%), increased transaminases (28%), and hyponatremia (18%).

Dosage form and strength: 100 mg/4 mL (25 mg/mL) solution in single-dose vial

Preparation for intravenous infusion

1. Visually inspect the solution for particulate matter and discoloration. The solution is clear to slightly opalescent, colorless to slightly yellow. Discard the vial if visible particles are observed.

2. Dilute KEYTRUDA injection (solution) prior to intravenous administration.

3. Withdraw the required volume from the vial of KEYTRUDA and transfer into an intravenous (IV) bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP. Mix diluted solution by gentle inversion. Do not shake. The final concentration of the diluted solution should be between 1 mg/mL to 10 mg/mL.

4. Discard any unused portion left in the vial.

Storage of diluted solution

• The product does not contain a preservative.

• Store the diluted solution from the KEYTRUDA 100 mg/mL vial either:
  – At room temperature for no more than 6 hours from the time of dilution. This includes room temperature storage of the infusion solution in the IV bag, and the duration of infusion.
  – Under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 96 hours from the time of dilution. If refrigerated, allow the diluted solution to come to room temperature prior to administration. Do not shake.

• Discard after 6 hours at room temperature or after 96 hours under refrigeration.

• Do not freeze.

1. Administer diluted solution intravenously over 30 minutes through an intravenous line containing a sterile, non-pyrogenic, low-protein binding 0.2 micron to 5 micron in-line or add-on filter.

2. Do not co-administer other drugs through the same infusion line.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.
Pneumonitis
• Monitor for signs and symptoms of pneumonitis.
• Evaluate suspected pneumonitis with radiographic imaging.
• Administer corticosteroids for Grade 2 or greater pneumonitis.
• Withhold KEYTRUDA for Grade 2 pneumonitis; permanently discontinue KEYTRUDA for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

Colitis
• Monitor for signs and symptoms of colitis.
• Administer corticosteroids for Grade 2 or greater colitis.
• Withhold KEYTRUDA for Grade 2 or 3 colitis; permanently discontinue KEYTRUDA for Grade 4 colitis.

Hepatitis
• Monitor for changes in liver function.
• Administer corticosteroids for Grade 2 or greater hepatitis, based on severity of liver enzyme elevations, withholding or discontinuing KEYTRUDA.
• Please refer to the dose modifications information on page 14 for specific guidance for patients with HCC.

Talk with your patients about immune-mediated and other adverse reactions that can occur during treatment with KEYTRUDA (continued).

Endocrinopathies
• Monitor for signs and symptoms of adrenal insufficiency, hypophysitis (including hypopituitarism), changes in thyroid function (prior to and periodically during treatment), and hyperglycemia.
• For adrenal insufficiency or hypophysitis, administer corticosteroids and hormone replacement as clinically indicated. Withhold KEYTRUDA for Grade 2 adrenal insufficiency or hypophysitis; withhold or discontinue KEYTRUDA for Grade 3 or 4 adrenal insufficiency or hypophysitis.
• Administer hormone replacement for hypothyroidism and manage hyperthyroidism with thionamides and beta-blockers as appropriate. Withhold or discontinue KEYTRUDA for Grade 3 or 4 hyperthyroidism.
• Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer antihyperglycemics in patients with severe hyperglycemia.
Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue in patients receiving KEYTRUDA. While these reactions usually occur during treatment, they may occur after discontinuation of treatment. For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold KEYTRUDA and administer corticosteroids or permanently discontinue KEYTRUDA.

**Monitoring**

**for adverse reactions (continued)**

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Monitoring patients</th>
<th>Management of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-adverse reactions</td>
<td>• Monitor for suspected immune skin reactions and exclude other causes.</td>
<td>• Based on the severity of the adverse reaction, withhold or permanently discontinue KEYTRUDA and administer corticosteroids or permanently discontinue KEYTRUDA.</td>
</tr>
<tr>
<td>• Increase or new-onset adverse reactions, whether occurring on or after treatment, can occur in any organ system or tissue in patients receiving KEYTRUDA and may occur after discontinuation of treatment. For suspected non-adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• For suspected non-adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• In patients with solid organ transplants, consider the benefit of treatment with KEYTRUDA versus the risk of a possible organ rejection.</td>
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</tbody>
</table>

**Talk with your patients about immune-mediated and other adverse reactions that can occur during treatment with KEYTRUDA (continued)**

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Monitoring patients</th>
<th>Management of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatotoxicity in combination with axitinib</td>
<td>• Monitor liver enzymes before initiation of and periodically throughout treatment.</td>
<td>• Consider more frequent monitoring of liver enzymes as compared to when the drugs are administered as single agents.</td>
</tr>
<tr>
<td>• For elevated liver enzymes, interrupt KEYTRUDA and axitinib, and consider administering corticosteroids as needed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>• Monitor for signs and symptoms of infusion-related reactions including rigors, chills, flushing, pruritus, and hypotension.</td>
<td>• For Grade 1 or 2 reactions, interrupt or slow the rate of infusion.</td>
</tr>
<tr>
<td>• For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergenic HSCT after treatment with KEYTRUDA</td>
<td>• Follow patients closely for evidence of transplant-related complications such as hyperacute GVHD, acute GVHD requiring steroid therapy, hepatic VOD, and other immune-mediated adverse reactions.</td>
<td></td>
</tr>
<tr>
<td>• For patients with early evidence of transplant-related complications, ensure adequate evaluation of liver function and continue to monitor for evidence of transplant-related complications.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Preserve immunosuppression with KEYTRUDA, and for suspected immune-mediated adverse reactions, ensure adequate evaluation of liver function and continue to monitor for evidence of transplant-related complications.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• In patients with solid organ transplants, consider the benefit of treatment with KEYTRUDA versus the risk of a possible organ rejection.</td>
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</tr>
</tbody>
</table>

**SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis; GVHD = graft-versus-host disease; VOD = veno-occlusive disease.**

**Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.**
For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold or discontinue KEYTRUDA and administer corticosteroids, as recommended below.

### Recommended Dose Modifications

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Severity</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune-mediated pneumonitis</td>
<td>Grade 2</td>
<td>Withhold</td>
</tr>
<tr>
<td>Grades 3 or 4</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Immune-mediated colitis</td>
<td>Grades 2 or 3</td>
<td>Withhold</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Immune-mediated hepatitis in patients with HCC</td>
<td>AST or ALT greater than or equal to 5 times ULN if baseline less than 2 times ULN, or &gt;3 times baseline if baseline greater than or equal to 2 times ULN</td>
<td>Withhold</td>
</tr>
<tr>
<td>Total bilirubin greater than 2.0 mg/dL if baseline less than 1.5 mg/dL</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>ALT or AST greater than 10 times ULN, or Child-Pugh score greater than or equal to 9 points</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Immune-mediated hepatitis in patients without HCC</td>
<td>AST or ALT greater than 3 but no more than 5 times the ULN or total bilirubin greater than 1.5 but no more than 3 times the ULN</td>
<td>Withhold</td>
</tr>
<tr>
<td>In patients with liver metastasis and Grade 2 AST or ALT at baseline, with an increase in AST or ALT of 50% or more relative to baseline that persists for at least 1 week</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Immune-mediated nephritis</td>
<td>Grade 2</td>
<td>Withhold</td>
</tr>
<tr>
<td>Grades 3 or 4</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Immune-mediated skin adverse reactions</td>
<td>Grade 3 or suspected SJS or TEN</td>
<td>Withhold</td>
</tr>
<tr>
<td>Grade 4 or confirmed SJS or TEN</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Hematologic toxicity in patients with vHL or pRCC</td>
<td>Grade 3</td>
<td>Withhold and resolution to Grade 1 or 2</td>
</tr>
<tr>
<td>Immune-mediated endocrinopathies</td>
<td>Grades 2 or 3</td>
<td>Withhold</td>
</tr>
</tbody>
</table>

**Adverse reaction Severity**

- **Grade 2**: Toxicity is manageable with dose modification and may resolve with medical treatment.
- **Grade 3**: Toxicity is significant but manageable with dose modification and may resolve with medical treatment.
- **Grade 4**: Toxicity is severe and life-threatening and may require hospitalization or life support.

**Dose Modification**

- **Withhold**: withhold treatment until toxicity resolves to Grade 0–1.
- **Permanently discontinue**: discontinue treatment immediately.

**Note:**

- AST = aspartate aminotransferase; ALT = alanine aminotransferase; ULN = upper limit of normal.
- Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE v4).
- Resume in patients with complete or partial resolution (Grades 0 to 1) after corticosteroid taper.
- Resume in patients with HCC when AST or ALT and total bilirubin recover to Grades 0–1 or to baseline.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide is also available.
Selected Immune-mediated Adverse Reactions

Adverse Reaction          KEYTRUDA
(N=2,799)  

All Grades          Grade 3          Grade 4          Grade 5

Pneumonitis          3.4 (94)          0.9          0.3          0.1

Pneumonitis in NSCLC  (N=790)          8.2 (65)          3.2          –          –

Pneumonitis in HNSCC  (monotherapy)  (N=300)          6.0 (18)          1.3          –          0.3

Pneumonitis in HNSCC  (combination with platinum and FU)  (N=276)          5.4 (15)          1.1          –          0.4

Colitis              1.7 (48)          1.1 <0.1          –          –

Hepatitis            0.7 (19)          0.4 <0.1          –          –

Adrenal Insufficiency 0.8 (20)          0.3 <0.1          –          –

Hyperthyroidism      0.6 (17)          0.3 <0.1          –          –

Hypothyroidism       0.5 (15)          0.3 <0.1          –          –

Hypothyroidism in    0.5 (10)          0.1            –          –

HNSCC (monotherapy and combination with platinum and FU)  (N=1,185)          16 (188)          0.3          –          –

Nephritis            0.3 (9)          0.1 <0.1          –          –

Grades 3–4.

• Pneumonitis occurred more frequently in patients with a history of prior thoracic radiation. 8.4% compared to those without 2.8%.
• Pneumonitis occurred in 3.4% of patients with advanced NSCLC and a history of prior thoracic radiation vs 2.7% of patients who did not receive prior thoracic radiation.

When KEYTRUDA was used in combination with chemotherapy, the most common adverse reactions (≥20%) were fatigue/asthenia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, pyrexia, peripheral neurotoxicity, mucosal inflammation, and stomatitis.

When KEYTRUDA was used in combination with antibiotics, the most common adverse reactions (≥20%) were diarrhea, fatigue, anemia, neutropenia, hypotension, hyperglycemia, hyperkalemia, hypophosphatemia, decreased appetite, paronychia, skin infarction, rash, stomatitis, mucosal inflammation, dysphonia, cough, and constipation.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide is also available.

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• KEYTRUDA in combination with adriamycin can cause hepatoxicity with higher than expected frequencies of Grades 3 and 4 ALT and AST elevations compared to KEYTRUDA alone. Grades 3 and 4 AST were seen in 20% and 7% of patients, respectively.

• Immune-mediated rash, including SJS, TEN (some cases with fatal outcome), exfoliative dermatitis, and bullous pemphigoid, can occur with KEYTRUDA.

• The following clinically significant immune-mediated adverse reactions occurred in ≤0.1% of patients treated with KEYTRUDA: acute myocardial infarction, myocarditis, Guillain-Barré syndrome, myopathy, grade 3 or 4 hypertension, and hyperuricemia.

• Immune-mediated rashes, including SJS, TEN (some cases with fatal outcome), exfoliative dermatitis, and bullous pemphigoid, can occur with KEYTRUDA.

• The following clinically significant immune-mediated adverse reactions occurred in ≤0.1% of patients treated with KEYTRUDA: acute myocardial infarction, myocarditis, Guillain-Barré syndrome, myopathy, grade 3 or 4 hypertension, and hyperuricemia.

• In patients with a history of allogeneic HSCT, acute GVHD, including fatal GVHD, has been reported after treatment with KEYTRUDA. Patients who experienced GVHD after their transplant procedure may be at increased risk for GVHD after treatment with KEYTRUDA.

• In trials in patients with multiple myeloma, the addition of KEYTRUDA to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of these patients with a PD-1 or PD-L1 blocking antibody in this combination is not recommended outside of controlled trials.

• Treatment with KEYTRUDA may increase the risk of rejection in solid organ transplant recipients.

• KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% (6/2,799) of patients.

• Immune-mediated complications, including fatal events, occurred in patients who underwent allogeneic HSCT after treatment with KEYTRUDA. Of 23 patients with cHL who proceeded to allogeneic HSCT after KEYTRUDA, 6 (26%) developed GVHD (1 fatal case), and 2 (9%) developed severe hepatic VOD after reduced-intensity conditioning. GVHD and VOD have been reported in patients with lymphoma who received a PD-1 receptor-blocking antibody before transplantation.

• In patients with a history of allogeneic HSCT, acute GVHD, including fatal GVHD, has been reported after treatment with KEYTRUDA. Patients who experienced GVHD after their transplant procedure may be at increased risk for GVHD after treatment with KEYTRUDA.

• In trials in patients with multiple myeloma, the addition of KEYTRUDA to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of these patients with a PD-1 or PD-L1 blocking antibody in this combination is not recommended outside of controlled trials.

Common Adverse Reactions

When KEYTRUDA was used as monotherapy, the most common adverse reactions (≥20%) were fatigue, musculoskeletal pain, decreased appetite, pruritus, diarrhea, nausea, rash, perioral, cough, diarrhea, constipation, pain, and abdominal pain.

When KEYTRUDA was used in combination with chemotherapy, the most common adverse reactions (≥20%) were fatigue, anemia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, pyrexia, peripheral neuropathy, mucosal inflammation, and stomatitis.

When KEYTRUDA was used in combination with antibiotics, the most common adverse reactions (≥20%) were diarrhea, fatigue, anemia, hypotension, hyperkalemia, hypophosphatemia, decreased appetite, paronychia, skin infarction, rash, stomatitis, mucosal inflammation, dysphonia, cough, and constipation.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide is also available.
With KEYTRUDA, Merck provides resources for health care professionals and patients

**HEALTHCARE PROFESSIONAL RESOURCES**

- In-person nurse educators
- Merck sales representatives
- downloadable resources at keytrudashop.com

**PATIENT SUPPORT**

- The KEYYOU Patient Support Program offers 24/7 telephone support for eligible patients, referrals to organizations, and educational materials.

**PRODUCT ACCESS**

**THE MERCK ACCESS PROGRAM**

- may be able to help answer questions about:
  - Benefit investigations
  - Billing and coding
  - Co-pay assistance for eligible patients
  - Prior authorizations and appeals
  - Referral to the Merck Patient Assistance Program for eligibility determination (provided through the Merck Patient Assistance Program, Inc.)
  - Product distribution

For more information, visit merckaccessprogram-keytruda.com

For more information about access and support, call The Merck Access Program at 855-267-3832 (Monday to Friday, 8 AM to 8 PM).

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.
DISCUSS
Talking with your patients: KEYTRUDA is an immunotherapy that works with the body’s immune system to help fight cancer.2 KEYTRUDA can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death.

Understanding Immunotherapy With KEYTRUDA
"If you have received cancer therapies before, your experience during treatment with KEYTRUDA may be different. It is important for you to tell your cancer care team if you experience a side effect that bothers you or does not go away, as it could be a sign of a serious side effect."3

MANAGE
Management of adverse reactions includes identification and education of all those involved in the patient’s care. Patients receiving KEYTRUDA and their caregivers should be taught to recognize and report any signs and symptoms that may occur during treatment.3 Please consult pages 12 to 19 of this guide for information on the adverse reactions that can occur during treatment with KEYTRUDA.

Talking with your patients: Managing Symptoms With KEYTRUDA
"Communication is an important part of managing side effects. Stay in contact with your cancer care team."4

To learn more about managing adverse reactions or to download support resources, visit keytrudahcp.com
To learn more about KEYTRUDA, visit keytrudahcp.com

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

References: