Before prescribing KEYTRUDA, please read the accompanying Prescribing Information.

The Medication Guide also is available.
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**KEYTRUDA is approved for a range of patients**

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

### Cutaneous Squamous Cell Carcinoma
- KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic cutaneous 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.
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)

Classical Hodgkin Lymphoma
- KEYTRUDA is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL).
- KEYTRUDA is indicated for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

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. 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.

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.

Microsatellite Instability-High Cancers
- KEYTRUDA is indicated for the treatment of adult and pediatric patients with microsatellite instability-high (MSI-H) colorectal cancer or mismatch repair deficient (dMMR) colorectal cancer.

Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer
- KEYTRUDA is indicated for the first-line treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).
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 FDA-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 cancer of the esophagus whose tumors express PD-L1 (CPS ≥10) as determined by an FDA-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 ≥1) as determined by an FDA-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.

Triple-Negative Breast Cancer
- KEYTRUDA, in combination with chemotherapy, is indicated for the treatment of patients with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test. This indication is approved under accelerated approval based on progression-free survival. 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/neu = human epidermal growth factor receptor 2.
Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide is also available.

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.

TWO DOSING OPTIONS FOR KEYTRUDA

Choose an appropriate option for your patients

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

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 urethral carcinoma, MSI-H cancer (adult and pediatric), MSI-H/BRCA CRC, gastric cancer, esophageal cancer, cervical cancer, HCC, RCC (adult and pediatric), iSCC, or locally recurrent unresectable or metastatic TNBC: 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 (15 mg orally bid) should continue until disease progression, unacceptable toxicity, or for KEYTRUDA, up to 24 months. When axitinib is used in combination with KEYTRUDA, dose escalation of axitinib above the initial 15-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.

Gembrokatmib (Rupperl 0.1 mg)
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(s) 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/4 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.

Administration
1. Administer diluted solution intravenously over 30 minutes through an intravenous line containing a sterile, nonpyrogenic, 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.
Severe and Fatal Immune-Mediated Adverse Reactions

KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.

Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of anti–PD-1/PD-L1 treatments. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue KEYTRUDA depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy are discussed on the following pages.

Additional monitoring and management considerations for selected immune-mediated adverse reactions are also discussed.

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

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Monitoring and Management of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colitis</td>
<td>• Colitis may present with diarrhea.</td>
</tr>
<tr>
<td></td>
<td>• CMV infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.</td>
</tr>
<tr>
<td></td>
<td>• Monitor liver enzymes before initiation of and periodically throughout treatment.</td>
</tr>
<tr>
<td></td>
<td>• Consider more frequent monitoring of liver enzymes as compared to when the drugs are administered as single agents.</td>
</tr>
<tr>
<td></td>
<td>• For elevated liver enzymes, interrupt KEYTRUDA and steroids, and consider administering corticosteroids as needed.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Endocrinopathies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal insufficiency</td>
<td>• KEYTRUDA can cause primary or secondary adrenal insufficiency.</td>
</tr>
<tr>
<td></td>
<td>• For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td>• Withhold KEYTRUDA depending on severity.</td>
</tr>
<tr>
<td>Hypophysitis</td>
<td>• Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects.</td>
</tr>
<tr>
<td></td>
<td>• Hypophysitis can cause hypohyponadism.</td>
</tr>
<tr>
<td></td>
<td>• Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity.</td>
</tr>
<tr>
<td>Thyroid disorders</td>
<td>• Thyroiditis can present with or without exophthalmos.</td>
</tr>
<tr>
<td></td>
<td>• Hyperthyroidism can follow hypothyroidism.</td>
</tr>
<tr>
<td></td>
<td>• Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity.</td>
</tr>
</tbody>
</table>

| Type 1 diabetes mellitus | • Type 1 diabetes mellitus can present with diabetic ketonuria.  |
| Type 2 diabetes mellitus | • Monitor patients for hyperglycemia or other signs and symptoms of diabetes.  |
| Gestational diabetes | • Initiate treatment with insulin as clinically indicated. Withhold KEYTRUDA depending on severity. |

| Dermatologic adverse reactions | • Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate nonexfoliative rash. Withhold or permanently discontinue KEYTRUDA depending on severity. |

OMV = cytomegalovirus.
Dose Modifications

- No dose reduction for KEYTRUDA is recommended.
- In general, withhold KEYTRUDA for severe (Grade 3) immune-mediated adverse reactions.
- Permanently discontinue KEYTRUDA for:
  - Life-threatening Grade 4 immune-mediated adverse reactions.
  - Recurrent severe Grade 3 immune-mediated reactions that require systemic immunosuppressive treatment.
  - An inability to reduce concomitant dose to 10 mg or loss of prednisone or equivalent per day within 12 weeks of initiating steroids.
- Dosage modifications for KEYTRUDA are recommended when they differ from those general guidelines are summarized below.

### Recommended Dosage Modifications

#### Adverse Reaction | Severity | Dosage Modification
--- | --- | ---
Immune-mediated adverse reactions
- Pneumonitis
  - Grade 2
    - Reduce dose
  - Grade 3 or 4
    - Permanently discontinue

- Malignant colitis
  - Grade 3
    - Reduce dose
  - Grade 4
    - Permanently discontinue

- Hepatitis with tumor involvement of the liver
  - AST or ALT increases to more than 5 times ULN
    - Total bilirubin increases to more than 1.5 times ULN
      - Withhold or permanently discontinue
  - AST or ALT increases to more than 8 times ULN
    - Total bilirubin increases to more than 3 times ULN
      - Withhold or permanently discontinue

- Hepatitis with no tumor involvement of the liver
  - AST or ALT increases to more than 8 times ULN
    - Total bilirubin increases to more than 5 times ULN
      - Withhold or permanently discontinue
  - AST or ALT increases to more than 10 times ULN
    - Total bilirubin increases to more than 3 times ULN
      - Withhold or permanently discontinue

- Endocrinopathies
  - Grade 2 or 4
    - Withhold until clinically stable or permanently discontinue

---

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**Recommended Dosage Modifications (continued)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Adverse Reaction</th>
<th>Severity</th>
<th>Dosage Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>KEYTRUDA in combination with axitinib</td>
<td>Liver enzyme elevations*</td>
<td>~ALT or AST increases to at least 2 times ULN with concurrent total bilirubin increase to at least 2 times ULN</td>
<td>Withhold KEYTRUDA and axitinib until resolution to Grade 1 or 2</td>
</tr>
<tr>
<td></td>
<td>Liver enzyme elevations*</td>
<td>~ALT or AST increases to more than 3 times ULN with concurrent total bilirubin increase to at least 2 times ULN</td>
<td>Permanently discontinue KEYTRUDA and axitinib</td>
</tr>
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</table>

*Based on CTCAE, version 4.0.
- Consider corticosteroid therapy.
- Consider rechallenge with a single drug or sequential rechallenge with both drugs after resolution.

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**Selected Adverse Reactions**

**Incidence of Selected Immune-Mediated Adverse Reactions**

<table>
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<tr>
<th>Adverse Reaction</th>
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<tr>
<td></td>
<td>All Grades</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>3.4 (94)</td>
</tr>
<tr>
<td>Pneumonitis in cHL</td>
<td></td>
</tr>
<tr>
<td>(monotherapy) (N=389 adults)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>Colitis</td>
<td>1.7 (46)</td>
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<tr>
<td>Hepatitis</td>
<td>0.7 (19)</td>
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<tr>
<td>Adrenal insufficiency</td>
<td>0.8 (23)</td>
</tr>
<tr>
<td>Hypophysitis</td>
<td>0.6 (17)</td>
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<tr>
<td>Hyperthyroidism</td>
<td>3.4 (90)</td>
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<tr>
<td>Hypothyroidism</td>
<td>6 (237)</td>
</tr>
<tr>
<td>Hyperthyroidism in HNSCC (monotherapy and combination with platinum and FU) (N=1,188)</td>
<td>16 (188)</td>
</tr>
<tr>
<td>Nephritis</td>
<td>0.3 (9)</td>
</tr>
<tr>
<td>Dermatologic adverse reactions</td>
<td>1.4 (38)</td>
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**Dose Modifications (continued)**

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<td>Nephritis with renal dysfunction</td>
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<td>Exfoliative dermatologic conditions</td>
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<tr>
<td>Psoriasis</td>
<td>Grade 3 and 4</td>
<td>Withhold</td>
</tr>
<tr>
<td>Myositis</td>
<td>Grade 2, 3, or 4</td>
<td>Permanently discontinue</td>
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<td>Neurological toxicity</td>
<td>Grade 2 or 3</td>
<td>Withhold</td>
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<tr>
<td>Hematologic toxicity in patients with cHL or PMBCL</td>
<td>Grade 4</td>
<td>Withhold until resolution to Grade 0 or 1</td>
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---

**Other adverse reactions**

- Infusion-related reactions:
  - Grade 1 or 2: Interrupt or slow the rate of infusion
  - Grade 3 or 4: Permanently discontinue

---

**Recommended Specific Dosage Modifications for KEYTRUDA in Combination With Axitinib**

- The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.
- Pneumonitis rates for adult patients with cHL were similar in patients with and without prior thoracic radiation.
- The incidence of new or worsening hypothyroidism was higher in 389 adult patients with cHL (17%) receiving KEYTRUDA as a single agent, including Grade 1 (6.2%) and Grade 2 (10.8%) hypothyroidism.
- Of 1,269 patients receiving KEYTRUDA, thyroiditis occurred in 16 (0.6%) patients, including Grade 2 (0.3%), and type 1 diabetes mellitus, which can present with diabetic ketoacidosis, occurred in 6 (0.2%) patients.

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**Recommended Dosage Modifications (continued)**

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Management of Selected Immune-Mediated Adverse Reactions

**KEYTRUDA** *(N=2,799)*

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<tr>
<th>Adverse Reaction</th>
<th>Permanently Discontinued, % (n)</th>
<th>Withheld, % (n)</th>
<th>Systemic Corticosteroids, % (n/N)</th>
<th>Resolution Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonitis</td>
<td>1.3 (36)</td>
<td>0.9 (26)</td>
<td>67 (63/94)</td>
<td>50% of 94</td>
</tr>
<tr>
<td>Colitis</td>
<td>0.5 (15)</td>
<td>0.3 (13)</td>
<td>63 (33/18)</td>
<td>85% of 48</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>0.2 (6)</td>
<td>0.3 (8)</td>
<td>68 (13/19)</td>
<td>79% of 19</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>&lt;0.1 (1)</td>
<td>0.3 (8)</td>
<td>77 (17/22)</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>0.1 (4)</td>
<td>0.3 (7)</td>
<td>94 (18/27)</td>
<td></td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>0</td>
<td>&lt;0.1 (1)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>&lt;0.1 (2)</td>
<td>0.3 (7)</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Hypothyroidism</td>
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<td>0.3 (7)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Type 1 diabetes mellitus</td>
<td>&lt;0.1 (1)</td>
<td>0.3 (7)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Nephritis</td>
<td>0.1 (3)</td>
<td>0.3 (7)</td>
<td>89 (8/9)</td>
<td>56% of 9</td>
</tr>
<tr>
<td>Dermatologic adverse reactions</td>
<td>0.1 (2)</td>
<td>0.3 (7)</td>
<td>45 (15/38)</td>
<td>79% of 38</td>
</tr>
</tbody>
</table>

- Adult patients with SLE, who developed pneumonitis received high-dose corticosteroids for a median duration of 10 days (range: 2 days to 53 months). Pneumonitis led to discontinuation of KEYTRUDA in 5.4% (21) of patients. Of the patients who developed pneumonitis, 42% interrupted KEYTRUDA, 68% discontinued KEYTRUDA, and 77% had resolution.

- Additional immunosuppressant therapy was required in 4.2% of patients with colitis and in 11% of patients with hepatitis.

- Of those with adrenal insufficiency or hypothyroidism who required systemic corticosteroids, the majority of patients remained on systemic corticosteroids.

- The majority of patients with hypothyroidism required long-term thyroid hormone replacement.

- All patients who had type 1 diabetes mellitus required long-term insulin therapy.

- All patients who were without* systemic corticosteroids for a median duration of 11 days (range: 2 days to 53 months) had resolution.

- Of those who had resolution of pneumonitis or colitis:
  - None had recurrence of hepatitis or nephritis.
  - 6% had recurrence of dermatologic adverse reactions.

- KEYTRUDA in combination with axitinib can cause hepatic toxicity. With the combination of KEYTRUDA and axitinib, Grades 3 and 4 increased ALT (20%) and increased AST (10%) were seen at a higher frequency compared to KEYTRUDA alone.

- Fifty-nine percent of the patients with increased ALT received systemic corticosteroids.

- In patients with ALT ≥3 times ULN (Grades 2–4), ALT resolved to Grades 0–1 in 94%.

- Among the 92 patients who were rechallenged with either KEYTRUDA (n=3) or axitinib (n=89) administered as a single agent or with both (n=76), recurrence of ALT ≥3 times ULN was observed in 1 patient receiving KEYTRUDA, 16 patients receiving axitinib, and 24 patients receiving both.

- Fifty-nine percent of the patients with increased ALT ≥3 times ULN subsequently recovered from the event.

- KEYTRUDA can cause immune-mediated rash or dermatitis. Eosinophilic dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has occurred with anti–PD-1/PD-L1 treatments.

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA or were reported with the use of other anti–PD-1/PD-L1 treatments. Severe or fatal cases have been reported for some of these adverse reactions. Cardiac/Vascular: Myocarditis, pericarditis, vasculitis, Nonspecific Systemic Manifestations, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autonomic neuropathy, Ocular: Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairments, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss. Glaucoma/Choroidal Neutrophilic, to include increases in serum amylase and lipase levels, gastritis, duodenitis, Musculoskeletal and Connective Tissue: Tissue-Trypsin/Polypeptide, related to hepatitis, include renal failure, arthritis (1.5%), polymyalgia rheumatica, Systemic Inflammatory Response Syndrome, Histioytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

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

*This is applicable to all patients who were withheld KEYTRUDA due to the immune-mediated adverse reactions presented, except dermatitis.
Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

• Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti–PD-1/PD-L1 treatments. Transplant-related complications include hyperacute GvHD, acute and chronic GvHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between anti–PD-1/PD-L1 treatments and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefits vs risks of using anti–PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

• 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 an anti–PD-1/PD-L1 treatment 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, pyrexia, cough, dyspnea, constipation, pain, and abdominal pain.

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, atriope, peripheral neuropathy, mucosal inflammation, stomatitis, and headache.

When KEYTRUDA was used in combination with axitinib, the most common adverse reactions (≥20%) were diarrhea, fatigue/asthenia, hypertension, hepatotoxicity, hyperthyroidism, decreased appetite, palmar-planar erythrodysthesia, nausea, stomatitis/mucosal inflammation, dysphonia, rash, cough, and constipation.

SUPPORT RESOURCES FOR KEYTRUDA

KEYTRUDA: Resources for health care professionals and patients

HCP RESOURCES

• Downloadable resources at keytrudahcp.com

KEY+YOU

PATIENT SUPPORT

• The KEY+YOU Patient Support Program offers 24/7 telephone support for eligible patients, referrals to organizations, and educational materials.

If you have questions about KEYTRUDA, contact a sales representative or nurse educator.

THE MERCK ACCESS PROGRAM

may be able to help answer questions about:

• Benefit investigations
• Billing and coding
• Co-pay assistance for eligible patients
• The prior authorizations and appeals process
• 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 855-257-3932 (Monday to Friday, 8 AM to 8 PM).
Guide your patients through treatment with KEYTRUDA

**DISCUSS**

**Talking with your patients:**

KEYTRUDA is an immunotherapy that works with the body’s immune system to help fight cancer.¹

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.”¹

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

**START**

For Appropriate Patients, Start With KEYTRUDA:

• Identify patients appropriate for treatment with KEYTRUDA.
• Select the appropriate dose.
• Administer KEYTRUDA as an intravenous infusion over 30 minutes every 3 weeks or every 6 weeks as appropriate.
• Administer KEYTRUDA prior to chemotherapy when given on the same day.

**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.¹ Please consult pages 12 to 20 of this guide for information on the adverse reactions that can occur during treatment with KEYTRUDA.

Talking with your patients:

**Reporting Side Effects**

“Contact your cancer care team immediately if you have any symptoms of side effects. The sooner that side effects are reported, the sooner you can be treated.”¹

**Communications is an important part of managing side effects. Stay in contact with your cancer care team.”¹**

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

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References:

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