GUIDE FOR KEYTRUDA

Information about dosing, administration, ordering, and support

KEYTRUDA®
(pembrolizumab) Injection 100 mg

Before prescribing KEYTRUDA, please read the Selected Safety Information on pages 8 to 10 and the accompanying Prescribing Information. The Medication Guide also is available.
INDICATIONS AND USAGE FOR KEYTRUDA

- 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.
- 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 programmed death ligand 1 (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 small cell lung cancer (SCLC) with disease progression on or after platinum-containing 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.
- 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).
- KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [combined positive score (CPS) ≥1] as determined by an FDA-approved test.
- 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.
- 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 confirmatory trials.
- 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 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.

See additional indications for KEYTRUDA on page 3.

EGFR=epidermal growth factor receptor; ALK=anaplastic lymphoma kinase; FDA=Food and Drug Administration; FU=fluorouracil.

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• KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
  - solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
  - colorectal cancer that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan.
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. The safety and effectiveness of KEYTRUDA in pediatric patients with MSI-H central nervous system cancers have not been established.

• KEYTRUDA is indicated for the first-line treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).

• 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.

• KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma 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.

• 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.

• 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.

• 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.

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

• KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options. 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. The safety and effectiveness of KEYTRUDA in pediatric patients with TMB-H central nervous system cancers have not been established.

• 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.
DOSAGE AND ADMINISTRATION FOR KEYTRUDA

Patient Selection for NSCLC, HNSCC, Urothelial Carcinoma, Gastric Cancer, Esophageal Cancer, Cervical Cancer, MSI-H or dMMR Cancer, MSI-H or dMMR CRC, or TMB-H Cancer

Select patients for treatment with KEYTRUDA as a single agent based on the presence of positive PD-L1 expression in:

• stage III NSCLC who are not candidates for surgical resection or definitive chemoradiation.
• metastatic NSCLC.
• first-line treatment of metastatic or unresectable, recurrent HNSCC.
• metastatic urothelial carcinoma.
• metastatic gastric cancer. If PD-L1 expression is not detected in an archival gastric cancer specimen, evaluate the feasibility of obtaining a tumor biopsy for PD-L1 testing.
• metastatic esophageal cancer.
• recurrent or metastatic cervical cancer.

For the MSI-H/dMMR indications, select patients for treatment with KEYTRUDA as a single agent based on MSI-H/dMMR status in tumor specimens.

For the TMB-H indication, select patients for treatment with KEYTRUDA as a single agent based on TMB-H status in tumor specimens.

Because the effect of prior chemotherapy on test results for TMB-H, MSI-H, or dMMR in patients with high-grade gliomas is unclear, it is recommended to test for these markers in the primary tumor specimens obtained prior to initiation of temozolomide chemotherapy in patients with high-grade gliomas.

Information on FDA-approved tests for the detection of PD-L1 expression and TMB status is available at: http://www.fda.gov/CompanionDiagnostics. An FDA-approved test for the detection of MSI-H or dMMR is not currently available.

KEYTRUDA is indicated for use at an additional recommended dosage of 400 mg every 6 weeks for all approved adult indications. This indication 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.

FDA-Approved Dosing

Melanoma
The recommended dose of KEYTRUDA in adult patients with unresectable or metastatic melanoma is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until disease progression or unacceptable toxicity.

The recommended dose of KEYTRUDA for the adjuvant treatment of adult patients with melanoma is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until disease recurrence, unacceptable toxicity, or for up to 12 months.

NSCLC, HNSCC
The recommended dose of KEYTRUDA is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until disease progression, unacceptable toxicity, or up to 24 months.

When administering KEYTRUDA in combination with chemotherapy, administer KEYTRUDA prior to chemotherapy when given on the same day. Refer to the Prescribing Information for the chemotherapy agents administered in combination with KEYTRUDA for recommended dosing information, as appropriate.

SCLC, MSI-H or dMMR CRC, Gastric Cancer, Esophageal Cancer, Cervical Cancer, HCC, cSCC
The recommended dose of KEYTRUDA is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until disease progression, unacceptable toxicity, or up to 24 months.

cHL, PMBCL, MSI-H or dMMR Cancer, MCC, TMB-H Cancer
The recommended dose of KEYTRUDA in adults is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until disease progression or unacceptable toxicity, or up to 24 months.

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 until disease progression or unacceptable toxicity, or up to 24 months.

See additional FDA-approved dosing for KEYTRUDA on page 5.

Before prescribing KEYTRUDA, please read the Selected Safety Information on pages 8 to 10 and the accompanying Prescribing Information. The Medication Guide also is available.
DOSE MODIFICATIONS FOR KEYTRUDA

FDA-Approved Dosing (continued)

Urothelial Carcinoma

The recommended dose of KEYTRUDA in patients with locally advanced or metastatic urothelial carcinoma is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until disease progression or unacceptable toxicity, or up to 24 months.

The recommended dose of KEYTRUDA in patients with high-risk BCG-unresponsive NMIBC is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until persistent or recurrent high-risk NMIBC, disease progression or unacceptable toxicity, or up to 24 months.

RCC

The recommended dose of KEYTRUDA is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks in combination with axitinib 5 mg orally twice daily 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 5-mg dose may be considered at intervals of 6 weeks or longer. See also the Prescribing Information for recommended axitinib dosing information.

DOSAGE AND ADMINISTRATION FOR KEYTRUDA

DOSAGE AND ADMINISTRATION FOR KEYTRUDA (continued)

Urothelial Carcinoma

The recommended dose of KEYTRUDA in patients with locally advanced or metastatic urothelial carcinoma is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until disease progression or unacceptable toxicity, or up to 24 months.

The recommended dose of KEYTRUDA in patients with high-risk BCG-unresponsive NMIBC is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks until persistent or recurrent high-risk NMIBC, disease progression or unacceptable toxicity, or up to 24 months.

RCC

The recommended dose of KEYTRUDA is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks in combination with axitinib 5 mg orally twice daily 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 5-mg dose may be considered at intervals of 6 weeks or longer. See also the Prescribing Information for recommended axitinib dosing information.

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<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Severity</th>
<th>Dose Modification for KEYTRUDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune-mediated pneumonitis</td>
<td>Grade 2</td>
<td>Withhold&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Grades 3 or 4 or recurrent Grade 2</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Immune-mediated colitis</td>
<td>Grades 2 or 3</td>
<td>Withhold&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Immune-mediated hepatitis in patients with HCC</td>
<td>Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than or equal to 5 times upper limit of normal (ULN) if baseline less than 2 times ULN; AST or ALT greater than 3 times baseline if baseline greater than or equal to 2 times ULN; Total bilirubin greater than 2.0 mg/dL if baseline less than 1.5 mg/dL; or Total bilirubin greater than 3.0 mg/dL, regardless of baseline levels</td>
<td>Withhold&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>ALT or AST greater than 10 times ULN; or Child-Pugh score greater than or equal to 9 points; Gastrointestinal bleeding suggestive of portal hypertension; or New onset of clinically detectable ascites; or encephalopathy</td>
<td>Permanently discontinue</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&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>For liver enzyme elevations in RCC patients treated with combination therapy, see dosing guidelines following this table.</td>
<td>In patients without liver metastases, AST or ALT greater than 5 times ULN or total bilirubin greater than 3 times ULN 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>
</tr>
</tbody>
</table>

<sup>a</sup>Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events. Version 4.0 (NCI CTCAE v4)

<sup>b</sup>Resume in patients with complete or partial resolution (Grades 0 to 1) after corticosteroid taper.

<sup>c</sup>Resume in HCC patients when AST or ALT and total bilirubin recover to Grades 0-1 or to baseline.

See additional dose modifications for KEYTRUDA on page 6.

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### DOSE MODIFICATIONS FOR KEYTRUDA (continued)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Severity*</th>
<th>Dose Modification for KEYTRUDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune-mediated endocrinopathies</td>
<td>Grades 3 or 4</td>
<td>Withhold until clinically stable</td>
</tr>
<tr>
<td>Immune-mediated nephritis</td>
<td>Grade 2</td>
<td>Withhold</td>
</tr>
<tr>
<td></td>
<td>Grades 3 or 4</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Immune-mediated skin adverse reactions</td>
<td>Grade 3 or suspected Stevens-Johnson Syndrome (SJS) or toxic epidermal necrolysis (TEN)</td>
<td>Withhold</td>
</tr>
<tr>
<td></td>
<td>Grade 4 or confirmed SJS or TEN</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Hematologic toxicity in patients with cHL or PMBCL</td>
<td>Grade 4</td>
<td>Withhold until resolution to Grades 0 or 1</td>
</tr>
<tr>
<td>Other immune-mediated adverse reactions</td>
<td>Grades 2 or 3 based on the severity and type of reaction</td>
<td>Withhold</td>
</tr>
<tr>
<td></td>
<td>Grade 3 based on the severity and type of reaction or Grade 4</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Recurrent immune-mediated adverse reactions</td>
<td>Recurrent Grade 2 pneumonitis</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td></td>
<td>Recurrent Grades 3 or 4</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Inability to taper corticosteroid</td>
<td>Requirement for 10 mg per day or greater prednisone or equivalent for more than 12 weeks after last dose of KEYTRUDA</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Persistent Grade 2 or 3 adverse reaction (excluding endocrinopathy)</td>
<td>Grades 2 or 3 adverse reactions lasting 12 weeks or longer after last dose of KEYTRUDA</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>Grades 1 or 2</td>
<td>Interrupt or slow the rate of infusion</td>
</tr>
<tr>
<td></td>
<td>Grades 3 or 4</td>
<td>Permanently discontinue</td>
</tr>
</tbody>
</table>

*Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events. Version 4.0 (NCI CTCAE v4)

*Resume in patients with complete or partial resolution (Grades 0 to 1) after corticosteroid taper.

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.

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PREPARATION AND ADMINISTRATION FOR KEYTRUDA

Preparation for Intravenous Infusion

- 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.
- Dilute KEYTRUDA injection (solution) prior to intravenous administration.
- Withdraw the required volume from the vial(s) of KEYTRUDA and transfer into an intravenous 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.
- 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 diluted solution, 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

- 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.
- Do not co-administer other drugs through the same infusion line.
SELECTED SAFETY INFORMATION FOR KEYTRUDA

Immune-Mediated Pneumonitis
- KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 3.4% (94/2799) of patients with various cancers receiving KEYTRUDA, including Grade 1 (0.8%), 2 (1.3%), 3 (0.9%), 4 (0.3%), and 5 (0.1%). Pneumonitis occurred in 8.2% (65/790) of NSCLC patients receiving KEYTRUDA as a single agent, including Grades 3-4 in 3.2% of patients, and occurred more frequently in patients with a history of prior thoracic radiation (17%) compared to those without (7.7%). Pneumonitis occurred in 6% (18/300) of HNSCC patients receiving KEYTRUDA as a single agent, including Grades 3-5 in 1.6% of patients, and occurred in 5.4% (15/276) of patients receiving KEYTRUDA in combination with platinum and FU as first-line therapy for advanced disease, including Grades 3-5 in 1.5% of patients.

- Monitor patients 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; permanently discontinue KEYTRUDA for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

Immune-Mediated Colitis
- KEYTRUDA can cause immune-mediated colitis. Colitis occurred in 1.7% (48/2799) of patients receiving KEYTRUDA, including Grade 2 (0.4%), 3 (1.1%), and 4 (<0.1%). Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

Immune-Mediated Hepatitis (KEYTRUDA) and Hepatotoxicity (KEYTRUDA in Combination With Axitinib)

Immune-Mediated Hepatitis
- KEYTRUDA can cause immune-mediated hepatitis. Hepatitis occurred in 0.7% (19/2799) of patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.4%), and 4 (<0.1%). Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

Hepatotoxicity in Combination With Axitinib
- KEYTRUDA in combination with axitinib can cause hepatic toxicity with higher than expected frequencies of Grades 3 and 4 ALT and AST elevations compared to KEYTRUDA alone. With the combination of KEYTRUDA and axitinib, Grades 3 and 4 increased ALT (20%) and increased AST (13%) were seen. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider more frequent monitoring of liver enzymes as compared to when the drugs are administered as single agents. For elevated liver enzymes, interrupt KEYTRUDA and axitinib, and consider administering corticosteroids as needed.

Immune-Mediated Endocrinopathies
- KEYTRUDA can cause adrenal insufficiency (primary and secondary), hypophysitis, thyroid disorders, and type 1 diabetes mellitus. Adrenal insufficiency occurred in 0.8% (22/2799) of patients, including Grade 2 (0.3%), 3 (0.3%), and 4 (<0.1%). Hypophysitis occurred in 0.6% (17/2799) of patients, including Grade 2 (0.2%), 3 (0.3%), and 4 (<0.1%). Hypothyroidism occurred in 8.5% (237/2799) of patients, including Grade 2 (6.2%) and 3 (0.1%). The incidence of new or worsening hypothyroidism was higher in 1185 patients with HNSCC (16%) receiving KEYTRUDA, as a single agent or in combination with platinum and FU, including Grade 3 (0.3%) hypothyroidism. Hyperthyroidism occurred in 3.4% (96/2799) of patients, including Grade 2 (0.8%) and 3 (0.1%), and thyroiditis occurred in 0.6% (16/2799) of patients, including Grade 2 (0.3%). Type 1 diabetes mellitus, including diabetic ketoacidosis, occurred in 0.2% (6/2799) of patients.

- Monitor patients for signs and symptoms of adrenal insufficiency, hypophysitis (including hypopituitarism), 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 and 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 Nephritis and Renal Dysfunction
- KEYTRUDA can cause immune-mediated nephritis. Nephritis occurred in 0.3% (9/2799) of patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.1%), and 4 (<0.1%) nephritis. Nephritis occurred in 1.7% (7/405) of patients receiving KEYTRUDA in combination with pemetrexed and platinum chemotherapy. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue for Grade 3 or 4 nephritis.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.
SELECTED SAFETY INFORMATION FOR KEYTRUDA (continued)

Immune-Mediated Skin Reactions

- Immune-mediated rashes, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) (some cases with fatal outcome), exfoliative dermatitis, and bullous pemphigoid, can occur. Monitor patients for suspected severe skin reactions and based on the severity of the adverse reaction, withhold or permanently discontinue KEYTRUDA and administer corticosteroids. For signs or symptoms of SJS or TEN, withhold KEYTRUDA and refer the patient for specialized care for assessment and treatment. If SJS or TEN is confirmed, permanently discontinue KEYTRUDA.

Other Immune-Mediated Adverse Reactions

- Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue in patients receiving KEYTRUDA and may also 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. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Based on limited data from clinical studies in patients whose immune-related adverse reactions could not be controlled with corticosteroid use, administration of other systemic immunosuppressants can be considered. Resume KEYTRUDA when the adverse reaction remains at Grade 1 or less following corticosteroid taper. Permanently discontinue KEYTRUDA for any Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

- The following clinically significant immune-mediated adverse reactions occurred in less than 1% (unless otherwise indicated) of 2799 patients: arthritis (1.5%), uveitis, myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, sarcoidosis, and encephalitis. In addition, myelitis and myocardiitis were reported in other clinical trials, including classical syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, sarcoidosis, and encephalitis. In addition, myelitis and myocardiitis were reported in other clinical trials, including classical Hodgkin lymphoma, and postmarketing use.

- Treatment with KEYTRUDA may increase the risk of rejection in solid organ transplant recipients. Consider the benefit of treatment vs the risk of possible organ rejection in these patients.

Infusion-Related Reactions

- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% (6/2799) of patients. Monitor patients for signs and symptoms of infusion-related reactions. For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- 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 graft-versus-host disease (GVHD) (1 fatal case) and 2 (9%) developed severe hepatic veno-occlusive disease (VOD) after reduced-intensity conditioning (1 fatal case). Cases of fatal hyperacute GVHD after allogeneic HSCT have also been reported in patients with lymphoma who received a programmed death receptor-1 (PD-1) receptor–blocking antibody before transplantation. Follow patients closely for early evidence of transplant-related complications such as hyperacute GVHD, Grade 3 to 4 acute GVHD, steroid-requiring febrile syndrome, hepatic VOD, and other immune-mediated adverse reactions.

- 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 KEYTRUDA. Consider the benefit of KEYTRUDA vs the risk of GVHD in these patients.

Increased Mortality in Patients With Multiple Myeloma

- 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.

Embryofetal Toxicity

- 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.

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, alopecia, peripheral neuropathy, mucosal inflammation, and stomatitis.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.
SELECTED SAFETY INFORMATION FOR KEYTRUDA (continued)

Adverse Reactions (continued)

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

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 younger 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 these patients when compared to adults under 65 years of age were fatigue (45%), vomiting (38%), abdominal pain (28%), increased transaminases (28%), and hyponatremia (18%).
BILLING CODES AND NATIONAL DRUG CODES (NDCs) FOR KEYTRUDA

NDC and Packaging Information
The NDC is typically required when submitting a claim with a miscellaneous Healthcare Common Procedure Coding System (HCPCS) code. Please consult with the payer to understand specific billing requirements.

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>KEYTRUDA® (pembrolizumab) injection 100 mg</th>
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<tbody>
<tr>
<td>PACKAGE</td>
<td>NDC</td>
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<tr>
<td>Carton containing one 100 mg/4 mL (25 mg/mL), single-dose vial</td>
<td>0006-3026-02</td>
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<tr>
<td>Carton containing two 100 mg/4 mL (25 mg/mL), single-dose vials</td>
<td>0006-3026-04</td>
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</table>

Please note: The NDCs above are the billable NDCs that appear on the cartons. The NDC on the vial should not be used for billing purposes.


<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>DESCRIPTOR</th>
</tr>
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<tbody>
<tr>
<td>96413</td>
<td>Injection and Intravenous Infusion Chemotherapy and Other Highly Complex Drug or Highly Complex Biologic Agent Administration</td>
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</tbody>
</table>

*CPT Copyright 2020 American Medical Association. All rights reserved. Please consult with the applicable payer to understand the payer’s specific billing requirements.

HCPCS CODE FOR KEYTRUDA

<table>
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<th>HCPCS CODE</th>
<th>DESCRIPTOR</th>
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<tbody>
<tr>
<td>J9271</td>
<td>Injection, pembrolizumab, 1 mg</td>
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</table>

Information about HCPCS codes is based on guidance issued by the Centers for Medicare & Medicaid Services applicable to Medicare Part B and may not apply to other public or private payers. Resources containing possible codes that could be relevant for KEYTRUDA and its administration are available from The Merck Access Program. Please visit merckaccessprogram-keytruda.com or call 855-257-3932 to speak with a representative (Monday through Friday, 8 AM to 8 PM ET). You are solely responsible for determining the appropriate codes and for any action you take in billing. Please consult with the applicable payer to understand the payer’s specific billing requirements.

The information above may be relevant when billing for KEYTRUDA and its administration. This information is current as of July 2020. The information provided here is compiled from sources believed to be accurate, but Merck makes no representation that it is accurate. Consult the relevant manual and/or other guidelines for a description of each code to determine the appropriateness of its use and for information on additional codes. Diagnosis codes should be selected only by a health care professional. This information is subject to change. Merck cautions that payer-coding requirements vary and can frequently change, so it is important to regularly check with each payer or, where applicable, the Medicare Administrative Contractor as to payer-specific requirements.

You are solely responsible for determining the appropriate codes and for any action you take in billing. The information provided here is not intended to be definitive or exhaustive, and is not intended to replace the guidance of a qualified professional advisor. Diagnosis codes should be selected only by a health care professional. Merck and its agents make no warranties or guarantees, expressed or implied, concerning the accuracy or appropriateness of this information for your particular use given the frequent changes in public and private payer billing. The use of this information does not guarantee payment or that any payment received will cover your costs.

Before prescribing KEYTRUDA, please read the Selected Safety Information on pages 8 to 10 and the accompanying Prescribing Information. The Medication Guide also is available.
Authorized Distributors for KEYTRUDA

<table>
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<th>AUTHORIZED DISTRIBUTOR</th>
<th>PHONE NUMBER</th>
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<th>ORDER ITEM # FOR KEYTRUDA</th>
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<td>ASD Healthcare</td>
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<tr>
<td>Cardinal Health Specialty Distribution</td>
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<td>McKesson Specialty Care Distribution</td>
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<tr>
<td>Oncology Supply</td>
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<td>Carton of two 100 mg/4 mL (25 mg/mL), single-use vials</td>
<td>55356</td>
</tr>
</tbody>
</table>

Merck does not recommend the use of one authorized distributor over another. Merck does not make any warranty as to the services offered by any particular authorized distributor. The Supplemental Return Program for Oncology Products is available to eligible customers for eligible products purchased from a distributor. The program is subject to applicable conditions and restrictions. For information, please contact the Supplemental Returns Program for Oncology Products at 800-611-7397.

Before prescribing KEYTRUDA, please read the Selected Safety Information on pages 8 to 10 and the accompanying Prescribing Information. The Medication Guide also is available.
THE MERCK ACCESS PROGRAM FOR KEYTRUDA

The Merck Access Program can help answer questions about
- Benefit investigations
- Billing and coding
- Co-pay assistance for eligible patients
- The prior authorizations process
- Referral to the Merck Patient Assistance Program for eligibility determination (provided through the Merck Patient Assistance Program, Inc)
- Product distribution

Visit merckaccessprogram-keytruda.com or call 855-257-3932 to speak with a representative (available Monday through Friday, 8 AM to 8 PM ET).

NURSE EDUCATOR PROGRAM

Nurse educators provide nurse-to-nurse staff education on appropriate dosing and administration of KEYTRUDA and information to help offices understand how to manage any potential adverse events.

For questions about KEYTRUDA, call 855-257-3932 to request an appointment with a nurse educator.

To learn more about KEYTRUDA, please visit keytrudahcp.com.

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