

## NATIONAL DRUG CODE (NDC) AND BILLING AND DIAGNOSIS CODES FOR KEYTRUDA

The following codes may be relevant when billing for KEYTRUDA and its administration. This information is current as of August 2020. The information provided here is compiled from sources believed to be accurate, but Merck makes no representation that it is accurate. Information about HCPCS codes is based on guidance issued by the CMS applicable to Medicare Part B and may not apply to other public or private payers. 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.

### NDC and Packaging Information

The NDC is typically required when submitting a claim with a miscellaneous HCPCS code. Please consult with the payer to understand specific billing requirements.

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

**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.

### Billing Codes

Below is a list of possible codes that could be relevant for KEYTRUDA and its administration. Please consult with the applicable payer to understand the payer's specific billing requirements.

#### HCPCS Code for KEYTRUDA<sup>1</sup>

HCPCS CODE	DESCRIPTOR
J9271	Injection, pembrolizumab, 1 mg

#### Revenue Code—For Use in the Hospital Setting<sup>2</sup>

REVENUE CODE	DESCRIPTOR
0636	Drug requiring detailed coding

#### Current Procedural Terminology (CPT<sup>®</sup>)<sup>a</sup> Code for Administration<sup>3,4</sup>

CPT CODE	DESCRIPTOR
<b>96413</b> (Some payers may utilize 96365. Check with the applicable payer.)	Injection and Intravenous Infusion Chemotherapy and Other Highly Complex Drug or Highly Complex Biologic Agent Administration

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**Before prescribing KEYTRUDA, please read the Selected Safety Information on pages 4-6 and the accompanying [Prescribing Information](#). The [Medication Guide](#) also is available.**

## KEYTRUDA FOR ADVANCED NSCLC

The following codes as of August 2020 are provided as a reference and may be relevant when billing for KEYTRUDA and its administration. 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. You are solely responsible for determining the appropriate codes and for any action you take in billing.

When submitting a claim for KEYTRUDA, always verify coding requirements with the relevant payer. Coding requirements may vary by insurer or plan; please refer to the payer-specific policies to understand what may be covered.

Check with the relevant payer regarding guidance on which diagnoses they will recognize and the applicability of secondary codes. Health care professionals are solely responsible for selecting codes that appropriately reflect the patient's diagnosis, the services rendered, and the applicable payers' guidelines.

Providers should document the diagnosis with a sufficiently high degree of specificity based on the information available to enable the identification of the most appropriate code. Although CMS has said that an unspecified code may be appropriate in some cases, CMS has advised that you should always code with as much specificity as possible consistent with the clinical documentation.

Merck and its agents make no warranties concerning the accuracy or appropriateness of this information for your particular use given the frequent changes in public and private payer billing. 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. The use of this information does not guarantee payment or that any payment received will cover your costs.

**Indication**

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 epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (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 programmed death ligand 1 (PD-L1) [tumor proportion score (TPS)  $\geq 1\%$ ] 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  $\geq 1\%$ ) 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.

**FDA-Approved Dosing**

The FDA-approved dose of KEYTRUDA is either 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.

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.

**Before prescribing KEYTRUDA, please read the Selected Safety Information on pages 4-6 and the accompanying [Prescribing Information](#). The [Medication Guide](#) also is available.**

**KEYTRUDA**<sup>®</sup>  
(pembrolizumab) Injection 100 mg

### KEYTRUDA FOR ADVANCED NSCLC *(continued)*

#### Possible relevant diagnosis codes for NSCLC

C33: Malignant Neoplasm of Trachea<sup>5</sup>

ICD-10-CM CODE	DESCRIPTOR
<b>C33</b>	Malignant neoplasm of trachea

C34: Malignant Neoplasm of Bronchus and Lung<sup>5</sup>

The C34 series:

- *Excludes:* Kaposi's sarcoma of lung, malignant carcinoid tumor of the bronchus and lung

ICD-10-CM CODE	DESCRIPTOR
<b>C34.01</b>	Malignant neoplasm of right main bronchus
<b>C34.02</b>	Malignant neoplasm of left main bronchus
<b>C34.11</b>	Malignant neoplasm of upper lobe, right bronchus or lung
<b>C34.12</b>	Malignant neoplasm of upper lobe, left bronchus or lung
<b>C34.2</b>	Malignant neoplasm of middle lobe, bronchus or lung
<b>C34.31</b>	Malignant neoplasm of lower lobe, right bronchus or lung
<b>C34.32</b>	Malignant neoplasm of lower lobe, left bronchus or lung
<b>C34.81</b>	Malignant neoplasm of overlapping sites of right bronchus and lung
<b>C34.82</b>	Malignant neoplasm of overlapping sites of left bronchus and lung
<b>C34.91</b>	Malignant neoplasm of unspecified part of right bronchus or lung
<b>C34.92</b>	Malignant neoplasm of unspecified part of left bronchus or lung

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# CODING & BILLING

## SELECTED SAFETY INFORMATION

### 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 Grade 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.

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# CODING & BILLING

## SELECTED SAFETY INFORMATION (*continued*)

### 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.

### 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 myocarditis 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.

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# CODING & BILLING

## SELECTED SAFETY INFORMATION (*continued*)

### 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 ( $\geq 20\%$ ) 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 ( $\geq 20\%$ ) were fatigue/asthenia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, pyrexia, alopecia, peripheral neuropathy, mucosal inflammation, and stomatitis.
- When KEYTRUDA was used in combination with axitinib, the most common adverse reactions ( $\geq 20\%$ ) were diarrhea, fatigue/asthenia, hypertension, hepatotoxicity, hypothyroidism, decreased appetite, palmar-plantar erythrodysesthesia, nausea, stomatitis/mucosal inflammation, dysphonia, rash, cough, and constipation.
- When KEYTRUDA was used in combination with LENVIMA, the most common adverse reactions ( $\geq 20\%$ ) were fatigue, musculoskeletal pain, hypertension, diarrhea, decreased appetite, hypothyroidism, nausea, stomatitis, vomiting, decreased weight, abdominal pain, headache, constipation, urinary tract infection, dysphonia, hemorrhagic events, hypomagnesemia, palmar-plantar erythrodysesthesia syndrome, dyspnea, cough, and rash.

### 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 ( $\geq 15\%$  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%).

ALT=alanine aminotransferase; AST=aspartate aminotransferase; cHL=classical Hodgkin lymphoma; FU=fluorouracil; HNSCC=head and neck squamous cell carcinoma; NSCLC=non-small cell lung cancer; PD-L1=programmed death ligand 1.

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