KEYTRUDA® (pembrolizumab) Injection 100 mg

NOW APPROVED FOR 1ST-LINE TREATMENT OF
mNSCLC with high PD-L1 expression (TPS ≥50%)

KEYTRUDA® is indicated for the first-line treatment of patients with metastatic non–small cell lung cancer (mNSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS) ≥50%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

Dear Customer:

Merck is pleased to announce that KEYTRUDA is now the only anti–PD-1 approved for first-line treatment of mNSCLC with high PD-L1 expression (TPS ≥50%). In the KEYNOTE-024 study, KEYTRUDA demonstrated superior survival in the first-line treatment of mNSCLC vs platinum-containing chemotherapy in patients whose tumors expressed high levels of PD-L1 (TPS ≥50%).

• Superior OS: 40% reduction in the risk of death vs chemotherapy in mNSCLC with high PD-L1 expression (HR=0.60; 95% confidence interval [CI], 0.41–0.89; P=0.005).a
  – Results were based on a prespecified interim analysis conducted when 108 events (64% of the events needed for the final analysis) were observed (44 [29%] in the KEYTRUDA arm and 64 [42%] in the chemotherapy arm).
  – Median OS was not reached with KEYTRUDA (95% CI, NR–NR) or with chemotherapy (95% CI, 9.4–NR).

• Superior PFS: 50% reduction in the risk of progression or death vs chemotherapy in mNSCLC with high PD-L1 expression (HR=0.50; 95% CI, 0.37–0.68; P<0.001).
  – Number of events observed in each treatment arm: 73 (47%) with KEYTRUDA and 116 (77%) with chemotherapy.
  – 10.3-month median PFS with KEYTRUDA (95% CI, 6.7–NR) vs 6 months with chemotherapy (95% CI, 4.2–6.2).

• Objective response rate: 45% ORR with KEYTRUDA (95% CI, 37–53; P=0.001; n=69/154) vs 28% with chemotherapy (95% CI, 21–36; n=42/151).

• Median duration of response: Not reached with KEYTRUDA (range: 1.9+ to 14.5+ months) vs 6.3 months with chemotherapy (range: 2.1+ to 12.6+ months) at the time of analysis.1

KEYNOTE-024 study design*: A randomized (1:1), open-label, multicenter, active-controlled, phase 3 trial, which included treatment-naïve patients with mNSCLC whose tumors had high PD-L1 expression (TPS ≥50%). Patients with EGFR or ALK genomic tumor aberrations were ineligible. Patients were randomized to receive KEYTRUDA 200 mg Q3W (n=154) or investigator’s choice platinum-containing chemotherapy (n=151; including pemetrexed+carboplatin, pemetrexed+cisplatin, gemcitabine+cisplatin, gemcitabine+carboplatin, or paclitaxel+carboplatin; patients with nonsquamous NSCLC could receive pemetrexed maintenance). The major efficacy outcome measure was PFS. Additional efficacy outcome measures were OS and ORR. Patients on chemotherapy who experienced progression of disease were offered KEYTRUDA.

*a-P-value is compared with 0.0118 of the allocated alpha for this interim analysis.

ALK = anaplastic lymphoma kinase; EGFR = epidermal growth factor receptor; NR = not reached; ORR = objective response rate; OS = overall survival; PD-1 = programmed death receptor-1; PD-L1 = programmed death ligand 1; PFS = progression-free survival.

SELECTED SAFETY INFORMATION

• KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 94 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 1 (0.8%), 2 (1.3%), 3 (0.9%), 4 (0.3%), and 5 (0.1%) pneumonitis, and occurred more frequently in patients with a history of prior thoracic radiation (6.9%) compared to those without (2.9%). 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.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information on pages 2 and 3 and the accompanying Prescribing Information. The Medication Guide also is available.
KEYTRUDA can cause immune-mediated colitis. Colitis occurred in 48 (1.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.4%), 3 (1.1%), and 4 (0.1%) colitis. 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.

KEYTRUDA can cause immune-mediated hepatitis. Hepatitis occurred in 19 (0.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.4%), and 4 (<0.1%) hepatitis. 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.

KEYTRUDA can cause hypophysitis. Hypophysitis occurred in 17 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.2%), 3 (0.3%), and 4 (<0.1%) hypophysitis. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids and hormone replacement as clinically indicated. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3 or 4 hypophysitis.

KEYTRUDA can cause thyroid disorders, including hyperthyroidism, hypothyroidism, and thyroiditis. Hyperthyroidism occurred in 96 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.8%) and 3 (0.1%) hyperthyroidism. Hyperthyroidism occurred in 237 (8.5%) of 2799 patients receiving KEYTRUDA, including Grade 2 (6.2%) and 3 (0.1%) hypothyroidism. Thyroiditis occurred in 16 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.3%) thyroiditis. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer replacement hormones for hypothyroidism and manage hyperthyroidism with thionamides and beta-blockers as appropriate. Withhold or discontinue KEYTRUDA for Grade 3 or 4 hyperthyroidism.

KEYTRUDA can cause type 1 diabetes mellitus, including diabetic ketoacidosis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer antihyperglycemics in patients with severe hyperglycemia.

KEYTRUDA can cause immune-mediated nephritis. Nephritis occurred in 9 (0.3%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.1%), and 4 (0.1%) nephritis. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

KEYTRUDA can cause severe or life-threatening immune-mediated adverse reactions. 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 (1.1%), exfoliative dermatitis, bullous pemphigoid, rash (1.4%), uveitis, myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, and partial seizures arising in a patient with inflammatory foci in brain parenchyma.

KEYTRUDA can cause severe or life-threatening infusion-related reactions, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for signs and symptoms of infusion-related reactions, including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

KEYTRUDA was discontinued due to adverse reactions in 8% of 682 patients with metastatic NSCLC. The most common adverse event resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.8%). Adverse reactions leading to interruption of KEYTRUDA occurred in 23% of patients; the most common (≥1%) were diarrhea (1%), fatigue (1.3%), pneumonia (1%), liver enzyme elevation (1.2%), decreased appetite (1.2%), and pneumonitis (1%). The most common adverse reactions (occurring in at least 20% of patients and at a higher incidence than with docetaxel) were decreased appetite (25% vs 23%), dyspnea (23% vs 20%), and nausea (20% vs 18%).

It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA and for 4 months after the final dose.

Safety and effectiveness of KEYTRUDA have not been established in pediatric patients.
200-mg fixed-dose administration is now FDA-approved for the treatment of mNSCLC

The recommended dose of KEYTRUDA is 200 mg fixed dose administered as an intravenous infusion over 30 minutes Q3W until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. Selection of patients for treatment of mNSCLC with KEYTRUDA is based on the presence of positive PD-L1 expression.

Choose KEYTRUDA for first-line treatment of mNSCLC in patients with high PD-L1 expression.

Visit keytruda.com to download resources, learn more about testing for PD-L1 expression, and register to receive product updates.

The Merck Access Program

The Merck Access Program can address questions on:

- Billing and coding
- Co-pay assistance for eligible patients
- Benefit investigations
- Prior authorization and appeals
- Product distribution

More information is available at merckaccessprogram-keytruda.com. To learn more, call 855-257-3932 Monday to Friday, between 8 AM and 8 PM ET.

SELECTED SAFETY INFORMATION

- Immune-mediated adverse reactions occurred with KEYTRUDA, including pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis. Based on the severity of the adverse reaction, KEYTRUDA should be withheld or discontinued and corticosteroids administered if appropriate. For more information regarding immune-mediated adverse reactions, please read the additional Selected Safety Information inside this letter.

Before prescribing KEYTRUDA, please read the Selected Safety Information on pages 1–3 and the accompanying Prescribing Information. The Medication Guide also is available. For additional copies of the Prescribing Information, please call 800-672-6372, visit keytruda.com, or contact your Merck representative.