KEYTRUDA™
(pembrolizumab)

Healthcare Professional

Frequently Asked Questions

Important safety information to minimize the risk of immune-related adverse reactions

KEYTRUDA as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.

KEYTRUDA is indicated for the treatment of advanced non-small cell lung carcinoma (NSCLC) in adults whose tumours express PD-L1 and who have disease progression on or after prior chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should also have disease progression on approved therapy for these aberrations prior to receiving KEYTRUDA.

MSD

Before prescribing KEYTRUDA, please read the accompanying Summary of Product Characteristics.

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How should I **use this brochure?**

Please review the Summary of Product Characteristics for KEYTRUDA as well as this educational brochure prior to prescribing KEYTRUDA. Together, they will enable you to understand how KEYTRUDA is used, and will help you to:

- Understand potential adverse reactions
- Appropriately manage adverse reactions
- Utilize the Patient Information Brochure and Patient Alert Card with patients
- Ensure that adverse reactions are adequately and appropriately reported

The information in this brochure is provided by Merck Sharp & Dohme (MSD) for oncologists, oncology nurses, oncology pharmacists, and other Healthcare Professionals (HCPs) who are involved in the treatment of patients who are receiving KEYTRUDA. Healthcare professionals are asked to report any suspect adverse reactions. See page 9 of this brochure for how to report adverse reactions.

What is **KEYTRUDA™ (pembrolizumab)?**

KEYTRUDA is a medicine that helps the immune system to fight tumors. KEYTRUDA is a humanized monoclonal antibody that binds to the programmed death-1 (PD-1) receptor and blocks its interaction with ligands PD-L1 and PD-L2. The PD-1 receptor is a negative regulator of T-cell activity that has been shown to be involved in the control of T-cell immune responses. KEYTRUDA potentiates T-cell responses, including anti-tumor responses, through blockade of PD-1 binding to PD-L1 and PD-L2, which are expressed in antigen-presenting cells and may be expressed by tumors or other cells in the tumor microenvironment.

What is KEYTRUDA indicated for?

KEYTRUDA as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.
KEYTRUDA is indicated for the treatment of advanced non-small cell lung carcinoma (NSCLC) in adults whose tumours express PD-L1 and who have disease progression on or after prior chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should also have disease progression on approved therapy for these aberrations prior to receiving KEYTRUDA.

How is **KEYTRUDA administered?**

Treatment must be initiated and supervised by a specialist physician experienced in the treatment of cancer.

- The recommended dose of KEYTRUDA is 2 mg/kg administered intravenously over 30 minutes every 3 weeks. Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity.
- Atypical responses (ie, an initial transient increase in tumor size or small new lesions within the first few months, followed by tumor shrinkage) have been observed with KEYTRUDA.

It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until disease progression is confirmed.

Pregnancy and lactation

Advise women of childbearing potential that they should use effective contraception during treatment with KEYTRUDA and for at least 4 months after the last dose.

It is unknown whether KEYTRUDA is secreted in human milk. Since it is known that antibodies can be secreted in human milk, a risk to the newborns or infants cannot be excluded. A decision should be made whether to discontinue breast-feeding or to discontinue KEYTRUDA, taking into account the benefit of breast-feeding for the child and the benefit of KEYTRUDA therapy for the patient.

Pembrolizumab should not be used during pregnancy unless the clinical condition of the woman requires treatment with this medicine.

Adverse **reactions**

What adverse reactions may be associated with treatment with KEYTRUDA?

The safety of KEYTRUDA has been evaluated in 1,012 patients across 3 doses (2 mg/kg every 3 weeks or 10 mg/kg every 2 or 3 weeks) in clinical studies. In this patient population, the most common adverse reactions (>10%) with KEYTRUDA were diarrhea (15%), nausea (12%), pruritus (25%), rash (25%), arthralgia (13%), and fatigue (33%). The majority of

immune-related adverse reactions and severe infusion-related reactions.

Immune-related adverse reactions

Most immune-related adverse reactions occurring during treatment with KEYTRUDA were

and/or supportive care. Immune-related adverse reactions have also occurred after the last dose of KEYTRUDA.

The following immune-related adverse reactions have been reported in patients treated with KEYTRUDA:

- Immune-related pneumonitis
- Immune-related colitis
- Immune-related hepatitis
- Immune-related nephritis
- Immune-related endocrinopathies (including hypophysitis, type 1 diabetes mellitus, including diabetic ketoacidosis, hypothyroidism, hyperthyroidism, and thyroiditis)
- Other immune-related adverse reactions (uveitis, myositis, pancreatitis, and severe skin reactions)

Infusion-related reactions

Severe infusion-related reactions have been reported in patients receiving KEYTRUDA.

The frequencies of immune-related adverse reactions and infusion-related reactions are reported in section 4.8 of the Summary of Product Characteristics for KEYTRUDA.

Adverse reactions

How should I monitor for and manage immune-related adverse reactions in patients receiving KEYTRUDA™ (pembrolizumab)?

Discuss immune-related and other adverse reactions that can occur during treatment with KEYTRUDA with your patient prior to initiating treatment.

For suspected immune-related adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reactions:

corticosteroid taper and continue to taper over at least 1 month.

- Restart KEYTRUDA if the adverse reaction remains at Grade ≤1 within 12 weeks after last dose of KEYTRUDA and corticosteroid dose is ≤10 mg prednisone or equivalent per day.
- If any Grade 3 toxicity occurs a second time, permanently discontinue KEYTRUDA.
- 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.

	Monitor	Manage
Immune-related pneumonitis	• For signs and symptoms of pneumonitis. • Suspected pneumonitis should be confirmed with radiographic imaging and other causes excluded.	• Administer corticosteroids for Grade ≥2 events (initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper). • Withhold KEYTRUDA for Grade 2 pneumonitis. • Permanently discontinue KEYTRUDA for Grade 3, Grade 4, or recurrent Grade 2 pneumonitis.
Immune-related colitis	• For signs and symptoms of colitis; exclude other causes.	• Administer corticosteroids for Grade ≥2 events (initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper). • Withhold KEYTRUDA for Grade 2 or Grade 3 colitis. • Permanently discontinue KEYTRUDA for Grade 4 colitis.
hepatitis	during treatment, and as indicated based on clinical evaluation) and symptoms of hepatitis; exclude other causes.	• Administer corticosteroids: - Grade ≥3: 1–2 mg/kg/day prednisone or equivalent followed by a taper. • Based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.
Immune-related nephritis	• For changes in renal function; exclude other causes.	• Administer corticosteroids for Grade ≥2 events (initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper). • Based on severity of creatinine elevations: - Withhold KEYTRUDA for Grade 2. - Permanently discontinue KEYTRUDA for Grade 3 or Grade 4 nephritis.
Immune-related endocrinopathies	• For signs and symptoms of hypophysitis (including hypopituitarism and secondary adrenal insufficiency); exclude other causes. • For hyperglycemia or other signs and symptoms of diabetes. • For changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and clinical signs and symptoms of thyroid disorders.	• Long-term hormone replacement therapy may be necessary in cases of immune-related endocrinopathies. • Administer corticosteroids to treat secondary adrenal insufficiency and other hormone replacement as clinically indicated. • Withhold KEYTRUDA for symptomatic hypophysitis until the event is controlled with hormone replacement. is achieved. • Hypothyroidism may be managed with replacement therapy without treatment interruption or corticosteroids. • Hyperthyroidism may be managed symptomatically. Withhold or discontinue KEYTRUDA for Grade 3 or Grade 4 hyperthyroidism. • For patients with Grade 3 or Grade 4 hyperthyroidism that improved to Grade 2 or lower, continuation of KEYTRUDA may be considered, after corticosteroid taper, if needed. Thyroid function and hormone levels

Infusion-related reactions

Severe infusion-related reactions have been reported in patients receiving KEYTRUDA, including drug hypersensitivity, anaphylactic reaction, hypersensitivity, and cytokine release syndrome.

How should infusion-related reactions be treated?

- Patients with a mild or moderate infusion reaction may continue to receive KEYTRUDA with close monitoring.
- Premedication with antipyretic and antihistamine may be considered.

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How should I monitor for and manage immune-related adverse reactions in patients receiving KEYTRUDA™ (pembrolizumab)?

Discuss immune-related and other adverse reactions that can occur during treatment with KEYTRUDA with your patient prior to initiating treatment.

For suspected immune-related adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reactions:

corticosteroid taper and continue to taper over at least 1 month.

- Restart KEYTRUDA if the adverse reaction remains at Grade ≤1 within 12 weeks after last dose of KEYTRUDA and corticosteroid dose is ≤10 mg prednisone or equivalent per day.
- If any Grade 3 toxicity occurs a second time, permanently discontinue KEYTRUDA.
- 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.

Monitor

Immune-related pneumonitis	• For signs and symptoms of pneumonitis. • Suspected pneumonitis should be confirmed with radiographic imaging and other causes excluded.
Immune-related colitis	• For signs and symptoms of colitis; exclude other causes.
Immune-related hepatitis	• For changes in liver function (at the start of treatment, periodically symptoms of hepatitis; exclude other causes.
Immune-related nephritis	• For changes in renal function; exclude other causes.
Immune-related endocrinopathies	• For signs and symptoms of hypophysitis (including hypopituitarism and secondary adrenal insufficiency); exclude other causes. • For hyperglycemia or other signs and symptoms of diabetes. • For changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and clinical signs and symptoms of thyroid disorders.

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- Premedication with antipyretic and antihistamine may be considered.

Manage

Immune-related pneumonitis	• Administer corticosteroids for Grade ≥2 events (initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper). • Withhold KEYTRUDA for Grade 2 pneumonitis.
Immune-related colitis	• Administer corticosteroids for Grade ≥2 events (initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper). • Withhold KEYTRUDA for Grade 2 or Grade 3 colitis. • Permanently discontinue KEYTRUDA for Grade 4 colitis.
Immune-related hepatitis	• Administer corticosteroids: - Grade 2: initial dose of 0.5–1 mg/kg/day prednisone or equivalent followed by a taper. - Grade ≥3: 1–2 mg/kg/day prednisone or equivalent followed by a taper. • Based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.
Immune-related nephritis	followed by a taper). • Based on severity of creatinine elevations: - Withhold KEYTRUDA for Grade 2. - Permanently discontinue KEYTRUDA for Grade 3 or Grade 4 nephritis.
Immune-related endocrinopathies	

What is the **Patient Information Brochure?**

Important information about treatment with KEYTRUDA™ (pembrolizumab) has been highlighted in a Patient Information Brochure. You may use the brochure as a guide to help initiate a discussion with the patient about treatment. Patients can review on their own as needed to better understand their treatment regimen.

In addition to providing an overview of treatment, the Patient Information Brochure outlines precisely what the patient should do when experiencing an adverse reaction (ie, immune-mediated adverse reaction).

Included in each brochure is a Patient Alert Card, which patients must carry with them at all times and show at all medical visits to healthcare professionals other than the KEYTRUDA prescriber. Please direct the patient to complete all relevant sections of the card, including all contact information for the prescriber, patient, and any caregiver who plays a role in helping the patient. This card can be especially helpful in visits to emergency healthcare facilities, where the patient may be unknown.

Please take a moment to ensure patients understand how to use the Alert Card. See that it contains summary information about treatment and how to appropriately manage adverse reactions. Emphasize to patients the importance of completing the card and carrying it at all times.

Most importantly, patients should be reminded that if they do experience an adverse reaction, they should seek medical attention immediately and undergo prompt treatment.

Where can I **obtain further information?**

More information about KEYTRUDA is available in the Summary of Product Characteristics,

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

PLACEHOLDER: ADDRESS TO BE PROVIDED AT THE LOCAL LEVEL

Marketing Authorization Holder:
Merck Sharp & Dohme Limited
Hertford Road
Hoddesdon
Hertfordshire EN11 9BU
United Kingdom

Merck Sharp & Dohme Pharmacovigilance Saudi:
Merck Sharp & Dohme Scientific Office
Airport Road
Qurtubah, Business Gate, Building 3
P.O Box 13244, Riyadh
Fax: 00966114006484
Telephone: 00966112506719
email: saudi.pharmacovigilance@merck.com

To report any side effect(s):

- Saudi Arabia:

The National Pharmacovigilance and Drug Safety Centre (NPC), at SFDA
o Fax: +966-11-205-7662
o Call NPC at +966-11-20382222, Exts: 2317-2356-2353-2354-2334-2340.
o Toll free phone: 8002490000
o E-mail: npc.drug@sfda.gov.sa
o Website: www.sfda.gov.sa/npc

- Other GCC States:

Please contact the relevant competent authority.

For adults with advanced melanoma

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