# Managing immune-mediated adverse events for patients on KEYTRUDA[1]

KEYTRUDA® (pembrolizumab) for Injection 50 mg

**Contact the patient's treatment centre for advice.**

For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm aetiology or exclude other causes.

Assess patients for immune-mediated adverse reactions, particularly colitis, pneumonitis, hepatitis, nephritis and endocrinopathies.

Perform and evaluate laboratory tests as clinically indicated to confirm aetiology or exclude other causes.

## Symptom Checklist

Ask your patients if they have felt or noticed any changes in the following:

| ENDOCRINE SYSTEM | | | Please provide any details |
|---|---|---|---|
| Appetite changes? | ☐ NO | ☐ YES | |
| Weight changes? | ☐ NO | ☐ YES | |
| Drowsy, weak or extremely tired? | ☐ NO | ☐ YES | |
| Cold? | ☐ NO | ☐ YES | |
| Sweaty? | ☐ NO | ☐ YES | |
| Headaches? | ☐ NO | ☐ YES | |
| Dizziness or lightheaded? | ☐ NO | ☐ YES | |
| Changes in mood (e.g. irritability)? | ☐ NO | ☐ YES | |
| Rapid heartbeat? | ☐ NO | ☐ YES | |
| Flu-like symptoms? | ☐ NO | ☐ YES | |
| Muscles aches? | ☐ NO | ☐ YES | |

| PULMONARY AND CARDIOVASCULAR SYSTEM | | | Please provide any details |
|---|---|---|---|
| Coughing (either new or worsening)? | ☐ NO | ☐ YES | |
| Chest pain? | ☐ NO | ☐ YES | |
| Shortness of breath? | ☐ NO | ☐ YES | |

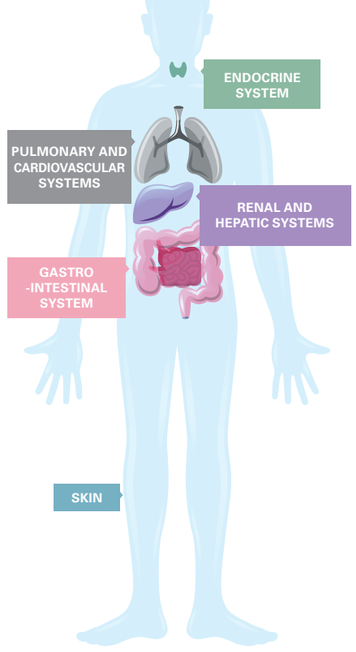
| SKIN | | | Please provide any details |
|---|---|---|---|
| Rash? | ☐ NO | ☐ YES | |
| Itches? | ☐ NO | ☐ YES | |
| Pigmentation or colour changes? | ☐ NO | ☐ YES | |
| Any other skin changes? | ☐ NO | ☐ YES | |

| GASTRO-INTESTINAL SYSTEMS | | | Please provide any details |
|---|---|---|---|
| Altered bowel habits (diarrhoea, constipation)? | ☐ NO | ☐ YES | # of movements/day: |
| Change in stool appearance (black, tar-like, blood, mucus-like)? | ☐ NO | ☐ YES | |
| Nausea? | ☐ NO | ☐ YES | |
| Vomiting? | ☐ NO | ☐ YES | |
| Stomach pains (e.g. tender or cramping)? | ☐ NO | ☐ YES | |

| RENAL AND HEPATIC SYSTEMS | | | Please provide any details |
|---|---|---|---|
| Change in urine quantity? | ☐ NO | ☐ YES | |
| Change in urine colour? | ☐ NO | ☐ YES | |
| Yellowing of skin and/or eyes? | ☐ NO | ☐ YES | |
| Swelling of ankles? | ☐ NO | ☐ YES | |
| Other bleeding, bruising or swelling? | ☐ NO | ☐ YES | |
| AST/ALT 1–3 x ULN or higher? | ☐ NO | ☐ YES | |

Note to Healthcare Professionals: Any organ can be affected. This checklist is not intended to replace clinical judgement. Please review the KEYTRUDA Data Sheet for further information. Should you wish to report a product complaint (including any adverse events), please email dpoc.australia@merck.com.

- KEYTRUDA side effects can occur at any time during or after treatment
- The following signs and symptoms may indicate immune-related side effects from treatment




| Adverse event[a] | Management | Follow-up |
|---|---|---|
| **Any Grade 1 (mild)** | **Supportive Care** | **Continue treatment with KEYTRUDA and monitor** |
| **Grade 2 (moderate):**<br>■ Pneumonitis ■ Nephritis<br>■ Hypophysitis[b]<br>**Grade 2 or 3 (moderate or severe)** colitis, other immune-mediated events<br>**Grade 3 (severe)** hyperthyroidism, symptomatic hypophysitis[b], severe skin reactions, SJS, TEN<br>**Grade 4 (life-threatening)** haematological toxicity | **Withhold treatment and administer corticosteroids**<br>■ Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month | **Resume treatment with KEYTRUDA when**<br>■ Adverse event recovers to Grade 0-1 within 12 weeks after last dose<br>■ Corticosteroid dose is reduced to ≤10 mg prednisolone or equivalent per day |
| **Hepatitis associated with**<br>■ AST/ALT >3 to 5 x ULN<br>■ Total bilirubin >1.5 to 3 x ULN | | |
| **Hepatitis associated with**<br>■ AST/ALT >5x ULN<br>■ AST/ALT increases ≥50% relative to baseline and lasts ≥1 week in patients with liver metastasis who begin treatment with moderate (Grade 2) elevation of AST/ALT<br>■ Total bilirubin >3 x ULN | **Permanently discontinue KEYTRUDA** | **Permanently discontinue KEYTRUDA when**<br>■ Adverse event does not resolve to Grade 0-1 within 12 weeks after last dose<br>■ Corticosteroid dosing cannot be reduced to≤10 mg prednisolone or equivalent per day<br>■ Any severe (Grade 3) treatment-related adverse event recurs |
| **Grade 3 or 4 (severe or life-threatening):**<br>■ Pneumonitis ■ Confirmed SJS<br>■ Nephritis ■ TEN<br>■ Infusion-related reaction ■ Myocarditis<br>■ Hypophysitis[b] ■ Colitis<br>■ Severe skin reactions<br>■ Other immune-mediated events<br>**Any Grade 4 (life-threatening) adverse event** | | |
| **Isolated hypothyroidism**<br>(Manage other thyroid disorders as described above by grade) | May be managed with replacement therapy, without KEYTRUDA treatment interruption and without corticosteroids | |

[a] Grades are defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE)v4.0; [b] Pituitary gland inflammation; ALT = alanine aminotransferase, AST = aspartate aminotransferase, ULN = upper limit of normal, SJS = Stevens-Johnson syndrome, TEN = toxic epidermal necrolysis.

Please report all adverse effects to our pharmacovigilance team at dpoc.australia@merck.com

Reference: 1. KEYTRUDA Data Sheet.

**KEYTRUDA (pembrolizumab) 50mg powder for infusion. Before prescribing KEYTRUDA, read the data sheet for information on dosage, contraindications, precautions, interactions and adverse effects available at www.medsafe.govt.nz or on request from Merck Sharp & Dohme (New Zealand) Limited. Prescription Only Medicine. Indication:** As monotherapy for the treatment of unresectable or metastatic melanoma in adults. In combination with platinum-pemetrexed for first-line treatment of metastatic non-squamous NSCLC. As monotherapy for first-line treatment of patients with metastatic NSCLC whose tumours express PD-L1 ≥50% tumour proportion score (TPS) on a validated test, with no EGFR or ALK genomic tumour aberrations. As monotherapy for the treatment of patients with advanced NSCLC with a PD-L1 TPS level ≥1% and who have received platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have received prior therapy for these aberrations prior to receiving KEYTRUDA. As monotherapy for refractory/ relapsed classical Hodgkin Lymphoma (cHL). As monotherapy for patients with locally advanced/ metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy, or who have received platinum-containing chemotherapy. See full data sheet. **Contraindications:** None. **Precautions:** Immune-mediated adverse reactions, including pneumonitis, colitis, hepatitis, nephritis, hypophysitis, type 1 diabetes mellitus, hyperthyroidism, hypothyroidism, thyroiditis, uveitis, myositis, Guillain-Barre syndrome, pancreatitis, encephalitis, sarcoidosis, myasthenic syndrome, severe skin reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis), and severe infusion reactions including hypersensitivity and anaphylaxis. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. For management of immune-mediated adverse events, see full data sheet. Limited information in patients with active infection and patients with on-going adverse reaction to ipilimumab – use caution. Acute graft-versus-host-disease in patients with history of allogeneic HSCT. Post-marketing: solid organ transplant rejection and myocarditis. See full data sheet for further information. **Interactions:** None expected. Avoid corticosteroids or immunosuppressants prior to treatment. **Side effects:** Clinical trials (treatment-related only): nasopharyngitis, anaemia, hypothyroidism, decreased appetite, dizziness, headache, cough, dyspnea, abdominal pain, constipation, diarrhea, nausea, vomiting, erythema, pruritus, rash, vitiligo, arthralgia, back pain, myalgia, pain in extremity, asthenia, chills, fatigue, oedema peripheral, pyrexia, colitis, hepatitis, hyperthyroidism, hypophysitis, nephritis, pneumonitis, type 1 diabetes mellitus, adrenal insufficiency, autoimmune hepatitis, alopecia, upper respiratory tract infection. **Dosage and administration:** The recommended dose of KEYTRUDA is 200 mg for previously untreated NSCLC, cHL, and urothelial carcinoma, and 2 mg/kg or 200 mg for melanoma or previously treated NSCLC (administered as an intravenous infusion over 30 minutes every 3 weeks). KEYTRUDA should be administered first when given in combination with pemetrexed and carboplatin. Treat with KEYTRUDA until disease progression or unacceptable toxicity. Atypical responses (i.e. an initial transient increase in tumour size or small new lesions followed by shrinkage) have been observed. Clinically stable patients (i.e. asymptomatic and not requiring urgent intervention) with initial evidence of progression can remain on treatment until confirmed. See full data sheet for further information, including details on PD-L1 testing KEYTRUDA is a funded medicine for melanoma patients– restrictions apply. KEYTRUDA is a private purchase medicine for NSCLC, cHL and urothelial carcinoma patients. Based on data sheet prepared 16 October 2017.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(pembrolizumab) for Injection 50mg