

# Managing immune-mediated adverse events for patients on KEYTRUDA<sup>1</sup>

## 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?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Weight changes?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Drowsy, weak or extremely tired?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Cold?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Sweaty?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Headaches?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Dizziness or lightheaded?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Changes in mood (e.g. irritability)?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Rapid heartbeat?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Flu-like symptoms?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Muscles aches?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____

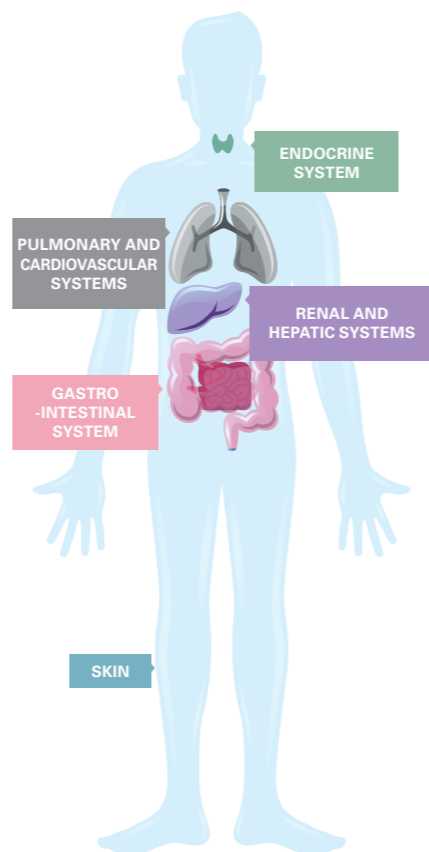
PULMONARY AND CARDIOVASCULAR SYSTEM		Please provide any details	
Coughing (either new or worsening)?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Chest pain?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Shortness of breath?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____

SKIN		Please provide any details	
Rash?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Itches?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Pigmentation or colour changes?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Any other skin changes?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____

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

RENAL AND HEPATIC SYSTEMS		Please provide any details	
Change in urine quantity?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Change in urine colour?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Yellowing of skin and/or eyes?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Swelling of ankles?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
Other bleeding, bruising or swelling?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____
AST/ALT 1-3 x ULN or higher?	<input type="checkbox"/> NO <input type="checkbox"/> YES	_____	_____

- 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<sup>a</sup>

Any Grade 1 (mild)

- Grade 2 (moderate):**
- Pneumonitis
  - Hypophysitis<sup>b</sup>
  - Nephritis
- Grade 2 or 3 (moderate or severe) colitis,** other immune-mediated events
- Grade 3 (severe) hyperthyroidism,** symptomatic hypophysitis<sup>b</sup>, severe skin reactions, SJS, TEN
- Grade 4 (life-threatening) haematological toxicity**

**Hepatitis associated with**

- AST/ALT >3 to 5 x ULN
- Total bilirubin >1.5 to 3 x ULN

**Hepatitis associated with**

- AST/ALT >5x ULN
- 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
- Total bilirubin >3 x ULN

**Grade 3 or 4 (severe or life-threatening):**

- Pneumonitis
- Nephritis
- Infusion-related reaction
- Hypophysitis<sup>b</sup>
- Severe skin reactions
- Other immune-mediated events
- Confirmed SJS
- TEN
- Myocarditis
- Colitis

**Any Grade 4 (life-threatening) adverse event**

**Isolated hypothyroidism**  
(Manage other thyroid disorders as described above by grade)

## Management

Supportive Care

**Withhold treatment and administer corticosteroids**

- Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month

**Permanently discontinue KEYTRUDA**

May be managed with replacement therapy, without KEYTRUDA treatment interruption and without corticosteroids

## Follow-up

**Continue treatment with KEYTRUDA and monitor**

**Resume treatment with KEYTRUDA when**

- Adverse event recovers to Grade 0-1 within 12 weeks after last dose
- Corticosteroid dose is reduced to ≤10 mg prednisolone or equivalent per day

**Permanently discontinue KEYTRUDA when**

- Adverse event does not resolve to Grade 0-1 within 12 weeks after last dose
- Corticosteroid dosing cannot be reduced to ≤10 mg prednisolone or equivalent per day
- Any severe (Grade 3) treatment-related adverse event recurs

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](http://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  $\geq 50\%$  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  $\geq 1\%$  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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**KEYTRUDA**<sup>®</sup>  
(pembrolizumab) for Injection 50mg