Identification of Common Adverse Reactions and Other Safety Information for KEYTRUDA® (pembrolizumab): A Focus on KEYNOTE-A39

KEYTRUDA, in combination with enfortumab vedotin (EV), is indicated for the treatment of adult patients with locally advanced (LA) or metastatic urothelial cancer (mUC).

KEYTRUDA® (pembrolizumab) Injection 100 mg

KEYNOTE-A39 Study Design

KEYNOTE-A39 was an open-label, randomized, multicenter trial that enrolled 886 patients with locally advanced or metastatic urothelial cancer who received no prior systemic therapy for locally advanced or metastatic disease. Patients with active central nervous system metastases, ongoing sensory or motor neuropathy Grade ≥2, or uncontrolled diabetes defined as hemoglobin A1C (HbA1c) ≥8% or HbA1c ≥7% with associated diabetes symptoms were excluded.

Patients were randomized 1:1 to receive either:

- KEYTRUDA 200 mg over 30 minutes on day 1 and enfortumab vedotin 1.25 mg/kg on days 1 and 8 of each 21-day cycle. KEYTRUDA was given approximately 30 minutes after enfortumab vedotin. Treatment was continued until disease progression or unacceptable toxicity. In the absence of disease progression or unacceptable toxicity, KEYTRUDA was continued for up to 2 years.
- Gemcitabine 1,000 mg/m^2 on days 1 and 8 of a 21-day cycle with cisplatin 70 mg/m^2 or carboplatin (area under the curve = 4.5 or 5) on day 1 of a 21-day cycle. Treatment was continued until disease progression or unacceptable toxicity for up to 6 cycles.

Randomization was stratified by cisplatin eligibility, programmed death ligand 1 (PD-L1) expression, and presence of liver metastases.

The median age was 69 years (range: 22 to 91); 77% were male; 67% were white, 22% were Asian, 1% were black or African American, and 10% were unknown or other; 12% were Hispanic or Latino. Patients had a baseline Eastern Cooperative Oncology Group performance status of 0 (49%), 1 (47%), or 2 (3%). Forty-seven percent of patients had a documented baseline HbA1c of <5.7%. At baseline, 95% of patients had metastatic urothelial cancer, including 72% with visceral and 22% with liver metastases, and 5% had locally advanced urothelial cancer. Eighty-five percent of patients had urothelial carcinoma histology including 6% with urothelial carcinoma mixed squamous differentiation and 2% with urothelial carcinoma mixed other histologic variants. Forty-six percent of patients were considered cisplatin-ineligible and 54% were considered cisplatin-eligible at time of randomization.

Visit keytrudahcp.com to see the complete list of approved indications for KEYTRUDA.

SELECTED SAFETY INFORMATION

SUMMARY OF IMMUNE-MEDIATED REACTIONS

- Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue and can affect more than one body system simultaneously. Immune-mediated adverse reactions can occur at any time during or after treatment with KEYTRUDA, including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis, dermatologic reactions, solid organ transplant rejection, other transplant (including corneal graft) rejection, and complications of allogeneic hematopoietic stem cell transplantation. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions. Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of KEYTRUDA. Based on the severity of the adverse reaction, KEYTRUDA should be withheld or permanently discontinued and corticosteroids administered if appropriate.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information on pages 2, 3 and 6–9 and the accompanying Prescribing Information. The Medication Guide also is available.

KEYTRUDA: Signs and Symptoms of Select Immune-Mediated and Other Adverse Reactions

Immune-mediated adverse reactions (IMARs), which may be severe or fatal, can occur in any organ system or tissue. The following are some signs and symptoms of select IMARs and other adverse reactions that patients should report. This is not an exhaustive list.

Pneumonitis

- Cough
- Shortness of breath
- Chest pain

Colitis

- Diarrhea (loose stools) or more frequent bowel movements than usual
- Stools that are black, tarry, sticky, or have blood or mucus
- Severe abdominal pain or tenderness

Hepatitis

- Jaundice
- Severe nausea or vomiting
- Pain on the right side of the abdomen
- Dark urine (tea colored)
- Easy bruising or bleeding

Dermatologic Adverse Reactions

- Rash
- Itching
- Skin blistering or peeling
- Painful sores or ulcers in the mouth, nose, throat, or genital area
- Fever or flu-like symptoms
- Swollen lymph nodes

Endocrinopathies

- Headaches that will not go away or unusual headaches
- Eye sensitivity to light
- Eye problems
- Rapid heartbeat
- Increased sweating
- Extreme tiredness
- Weight gain or weight loss
- Feeling more hungry or thirsty than usual
- Urinating more often than usual
- Hair loss
- Feeling cold
- Constipation
- Deepening voice
- Dizziness or fainting
- Changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Nephritis

- Decrease in the amount of urine
- Blood in the urine
- Swelling of the ankles
- Loss of appetite

Infusion-Related Reactions

- Chills or shaking
- Itching or rash
- Flushing
- Shortness of breath or wheezing
- Dizziness
- Feeling like passing out
- Fever
- Back pain

Signs and Symptoms of Select Immune-Mediated and Other Adverse Reactions continue on next page.

SELECTED SAFETY INFORMATION (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.

KEYTRUDA: Signs and Symptoms of Select Immune-Mediated and Other Adverse Reactions (*continued*)

Other clinically significant immune-mediated adverse reactions, some severe or fatal, can occur. The following are some signs and symptoms of other adverse reactions that patients should report. This is not an exhaustive list.

Other Immune-Mediated Adverse Reactions
• Chest pain, irregular heartbeat, shortness of breath, swelling of ankles • Confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs • Double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight • Persistent or severe muscle pain or weakness, muscle cramps • Low red blood cells, bruising

SELECTED SAFETY INFORMATION (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

- Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of anti–PD-1/PD-L1 treatments. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
- Withhold or permanently discontinue KEYTRUDA depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

- KEYTRUDA can cause immune-mediated pneumonitis. The incidence is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.4% (94/2799) of patients receiving KEYTRUDA, including fatal (0.1%), Grade 4 (0.3%), Grade 3 (0.9%), and Grade 2 (1.3%) reactions. Systemic corticosteroids were required in 67% (63/94) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 1.3% (36) and withholding in 0.9% (26) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Pneumonitis resolved in 59% of the 94 patients.

KEYNOTE-A39: Selected Adverse Reactions

The safety of KEYTRUDA in combination with enfortumab vedotin was investigated in KEYNOTE-A39 in patients with LA/mUC.

A total of 440 patients received KEYTRUDA 200 mg on day 1 and enfortumab vedotin 1.25 mg/kg on days 1 and 8 of each 21-day cycle compared with 433 patients who received gemcitabine on days 1 and 8 and investigator's choice of cisplatin or carboplatin on day 1 of each 21-day cycle.

Among patients who received KEYTRUDA and enfortumab vedotin, the median duration of exposure to KEYTRUDA was 8.5 months (range: 9 days to 28.5 months).

Fatal Adverse Reactions

Fatal adverse reactions occurred in 3.9% of patients treated with KEYTRUDA in combination with enfortumab vedotin, including:

- Acute respiratory failure (0.7%)
- Pneumonia (0.5%)
- Pneumonitis/ILD (0.2%)

Serious Adverse Reactions

Serious adverse reactions occurred in 50% of patients receiving KEYTRUDA in combination with enfortumab vedotin. Serious adverse reactions in ≥2% of patients receiving KEYTRUDA in combination with enfortumab vedotin were:

- Rash (6%)
- Acute kidney injury (5%)
- Pneumonitis/ILD (4.5%)
- Urinary tract infection (3.6%)
- Diarrhea (3.2%)
- Pneumonia (2.3%)
- Pyrexia (2%)
- Hyperglycemia (2%)

Permanent Discontinuation

Permanent discontinuation of KEYTRUDA occurred in 27% of patients. The most common adverse reactions (≥2%) resulting in permanent discontinuation of KEYTRUDA were:

- Pneumonitis/ILD (4.8%)
- Rash (3.4%)

Dose Interruptions

Dose interruptions of KEYTRUDA occurred in 61% of patients. The most common adverse reactions (≥2%) resulting in interruption of KEYTRUDA were:

- Rash (17%)
- Peripheral neuropathy (7%)
- COVID-19 (5%)
- Diarrhea (4.3%)
- Pneumonitis/ILD (3.6%)
- Neutropenia (3.4%)
- Fatigue (3%)
- Alanine aminotransferase increased (2.7%)
- Hyperglycemia (2.5%)
- Pneumonia (2%)
- Pruritus (2%)

ILD = interstitial lung disease; COVID-19 = Coronavirus Disease 2019.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information on pages 1–3 and 6–9 and the accompanying Prescribing Information. The Medication Guide also is available.

KEYNOTE-A39: Selected Adverse Reactions (*continued*)

Adverse Reactions ≥20% (All Grades) in Patients Treated With KEYTRUDA in Combination With Enfortumab Vedotin in KEYNOTE-A39

	KEYTRUDA in combination with enfortumab vedotin n=440		Chemotherapy n=433	
Adverse reaction	**All grades[a] %**	**Grades 3–4 %**	**All grades[a] %**	**Grades 3–4 %**
Skin and subcutaneous tissue disorders				
Rash[b]	68	15	15	0
Pruritus	41	1.1	7	0
Alopecia	35	0.5	8	0.2
General disorders and administration site conditions				
Fatigue[b]	51	6	57	7
Nervous system disorders				
Peripheral neuropathy[b]	67	8	14	0
Dysgeusia	21	0	9	0
Metabolism and nutrition disorders				
Decreased appetite	33	1.8	26	1.8
Gastrointestinal disorders				
Diarrhea	38	4.5	16	1.4
Nausea	26	1.6	41	2.8
Constipation	26	0	34	0.7
Investigations				
Weight loss	33	3.6	9	0.2
Eye disorders				
Dry eye[b]	24	0	2.1	0
Infections and infestations				
Urinary tract infection	21	5	19	8

Clinically relevant adverse reactions (<20%) include pyrexia (18%), dry skin (17%), vomiting (12%), pneumonitis/ILD (10%), hypothyroidism (10%), blurred vision (6%), infusion site extravasation (2%), and myositis (0.5%).

[a]Graded per NCI CTCAE v4.03.
[b]Includes multiple terms.
NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events.

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KEYNOTE-A39: Selected Laboratory Abnormalities

Selected Abnormalities Worsened From Baseline Occurring in ≥20% of Patients in KEYNOTE-A39

Laboratory test[a]	KEYTRUDA 200 mg every 3 weeks and enfortumab vedotin		Chemotherapy	
	All grades[b] %	Grades 3–4 %	All grades[b] %	Grades 3–4 %
Chemistry				
Increased aspartate aminotransferase	75	4.6	39	3.3
Increased creatinine	71	3.2	68	2.6
Hyperglycemia	66	14	54	4.7
Increased alanine aminotransferase	59	5	49	3.3
Hyponatremia	46	13	47	13
Hypophosphatemia	44	9	36	9
Hypoalbuminemia	39	1.8	35	0.5
Hypokalemia	26	5	16	3.1
Hyperkalemia	24	1.4	36	4.0
Hypercalcemia	21	1.2	14	0.2
Hematology				
Lymphopenia	58	15	59	17
Anemia	53	7	89	33
Neutropenia	30	9	80	50

[a]Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: KEYTRUDA (range: 407 to 439 patients).
[b]Graded per NCI CTCAE v4.03.

SELECTED SAFETY INFORMATION (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Immune-Mediated Colitis

- KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 1.7% (48/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (1.1%), and Grade 2 (0.4%) reactions. Systemic corticosteroids were required in 69% (33/48); additional immunosuppressant therapy was required in 4.2% of patients. Colitis led to permanent discontinuation of KEYTRUDA in 0.5% (15) and withholding in 0.5% (13) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Colitis resolved in 85% of the 48 patients.

SELECTED SAFETY INFORMATION (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Hepatotoxicity and Immune-Mediated Hepatitis

KEYTRUDA as a Single Agent

- KEYTRUDA can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 0.7% (19/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 68% (13/19) of patients; additional immunosuppressant therapy was required in 11% of patients. Hepatitis led to permanent discontinuation of KEYTRUDA in 0.2% (6) and withholding in 0.3% (9) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Hepatitis resolved in 79% of the 19 patients.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

- KEYTRUDA can cause primary or secondary adrenal insufficiency. For Grade 2 or higher, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.8% (22/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.3%) reactions. Systemic corticosteroids were required in 77% (17/22) of patients; of these, the majority remained on systemic corticosteroids. Adrenal insufficiency led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.3% (8) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Hypophysitis

- KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.6% (17/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 94% (16/17) of patients; of these, the majority remained on systemic corticosteroids. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Thyroid Disorders

- KEYTRUDA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Thyroiditis occurred in 0.6% (16/2799) of patients receiving KEYTRUDA, including Grade 2 (0.3%). None discontinued, but KEYTRUDA was withheld in <0.1% (1) of patients.
- Hyperthyroidism occurred in 3.4% (96/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.8%). It led to permanent discontinuation of KEYTRUDA in <0.1% (2) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement. Hypothyroidism occurred in 8% (237/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (6.2%). It led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.5% (14) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement. The majority of patients with hypothyroidism required long-term thyroid hormone replacement.

Type 1 Diabetes Mellitus (DM), Which Can Present With Diabetic Ketoacidosis

- Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1 DM occurred in 0.2% (6/2799) of patients receiving KEYTRUDA. It led to permanent discontinuation in <0.1% (1) and withholding of KEYTRUDA in <0.1% (1) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Immune-Mediated Nephritis With Renal Dysfunction

- KEYTRUDA can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (9/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.1%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 89% (8/9) of patients. Nephritis led to permanent discontinuation of KEYTRUDA in 0.1% (3) and withholding in 0.1% (3) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Nephritis resolved in 56% of the 9 patients.

SELECTED SAFETY INFORMATION (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Immune-Mediated Dermatologic Adverse Reactions

- KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has occurred with anti–PD-1/PD-L1 treatments. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate nonexfoliative rashes. Withhold or permanently discontinue KEYTRUDA depending on severity. Immune-mediated dermatologic adverse reactions occurred in 1.4% (38/2799) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 40% (15/38) of patients. These reactions led to permanent discontinuation in 0.1% (2) and withholding of KEYTRUDA in 0.6% (16) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 6% had recurrence. The reactions resolved in 79% of the 38 patients.

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA or were reported with the use of other anti–PD-1/PD-L1 treatments. Severe or fatal cases have been reported for some of these adverse reactions. *Cardiac/Vascular*: Myocarditis, pericarditis, vasculitis; *Nervous System*: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy; *Ocular*: Uveitis, iritis and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss; *Gastrointestinal*: Pancreatitis, to include increases in serum amylase and lipase levels, gastritis, duodenitis; *Musculoskeletal and Connective Tissue*: Myositis/polymyositis, rhabdomyolysis (and associated sequelae, including renal failure), arthritis (1.5%), polymyalgia rheumatica; *Endocrine*: Hypoparathyroidism; *Hematologic/Immune*: Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection, other transplant (including corneal graft) rejection.

Infusion-Related Reactions

- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% of 2799 patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti–PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute and chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between anti–PD-1/PD-L1 treatments and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefit vs risks of using anti–PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

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 an anti–PD-1/PD-L1 treatment 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.

SELECTED SAFETY INFORMATION (*continued*)

Adverse Reactions

- In KEYNOTE-A39, when KEYTRUDA was administered in combination with enfortumab vedotin to patients with locally advanced or metastatic urothelial cancer (n=440), fatal adverse reactions occurred in 3.9% of patients, including acute respiratory failure (0.7%), pneumonia (0.5%), and pneumonitis/ILD (0.2%). Serious adverse reactions occurred in 50% of patients receiving KEYTRUDA in combination with enfortumab vedotin; the serious adverse reactions in ≥2% of patients were rash (6%), acute kidney injury (5%), pneumonitis/ILD (4.5%), urinary tract infection (3.6%), diarrhea (3.2%), pneumonia (2.3%), pyrexia (2%), and hyperglycemia (2%). Permanent discontinuation of KEYTRUDA occurred in 27% of patients. The most common adverse reactions (≥2%) resulting in permanent discontinuation of KEYTRUDA were pneumonitis/ILD (4.8%) and rash (3.4%). The most common adverse reactions (≥20%) occurring in patients treated with KEYTRUDA in combination with enfortumab vedotin were rash (68%), peripheral neuropathy (67%), fatigue (51%), pruritus (41%), diarrhea (38%), alopecia (35%), weight loss (33%), decreased appetite (33%), nausea (26%), constipation (26%), dry eye (24%), dysgeusia (21%), and urinary tract infection (21%).

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 last dose.

Geriatric Use

- Of the 564 patients with locally advanced or metastatic urothelial cancer treated with KEYTRUDA in combination with enfortumab vedotin, 44% (n=247) were 65-74 years and 26% (n=144) were 75 years or older. No overall differences in safety or effectiveness were observed between patients 65 years of age or older and younger patients. Patients 75 years of age or older treated with KEYTRUDA in combination with enfortumab vedotin experienced a higher incidence of fatal adverse reactions than younger patients. The incidence of fatal adverse reactions was 4% in patients younger than 75 and 7% in patients 75 years or older.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information on pages 1–3 and 6–8 and the accompanying Prescribing Information. The Medication Guide also is available.

KEYTRUDA® (pembrolizumab) Injection 100 mg