Indications and Usage
IMFINZI is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:

- have disease progression during or following platinum-containing chemotherapy
- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
Dear Health Care Professional,

There are known serious immune-mediated safety risks associated with IMFINZI. Through proper knowledge and practice, you can help your patients manage their immune-mediated adverse events (imAEs).

- Early recognition and treatment of imAEs observed with IMFINZI can help keep imAEs from becoming more serious
- Routine monitoring of patients including routine lab tests during and after treatment is important

**IMFINZI™**

**durvalumab**

Injection for Intravenous Use 50 mg/mL

- Human programmed death ligand-1 (PD-L1) blocking antibody
- Blocks PD-L1 binding to PD-1 and CD80
- Helps overcome and prevent PD-L1–mediated inhibition of T-cell activation

Please see Important Safety Information on pages 37–38.
How to use this handbook

This handbook was created to inform you about the imAEs associated with IMFINZI and the management of these events. It is important to recognize and address signs and symptoms early. Management information for imAEs included in this handbook:

- Incidence of imAEs
- Signs and symptoms to recognize
- Management and dosing modification information
- Follow-up instructions

The 9 sections in this handbook include:

- Pulmonary
- Hepatic
- Gastrointestinal
- Endocrine
- Renal
- Skin
- Infection
- Infusion-related reactions
- Other

In addition to finding information by section, an index is included on the next page of this handbook listing individual imAEs.

Additional resources:

- Lighthouse-dedicated Advocate service (page 39)
- Immune-mediated Adverse Event Reminder Sheet (page 41)

Visit IMFINZI.com/hcp for more information
Index of imAEs

<table>
<thead>
<tr>
<th>Condition</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal insufficiency</td>
<td>19</td>
</tr>
<tr>
<td>Colitis</td>
<td>14</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>26</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>11</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>18</td>
</tr>
<tr>
<td>Hypophysitis/Hypopituitarism</td>
<td>19</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>17</td>
</tr>
<tr>
<td>Infection</td>
<td>29</td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>32</td>
</tr>
<tr>
<td>Nephritis</td>
<td>23</td>
</tr>
<tr>
<td>Other</td>
<td>34</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>8</td>
</tr>
<tr>
<td>Rash</td>
<td>26</td>
</tr>
<tr>
<td>Type 1 diabetes mellitus</td>
<td>20</td>
</tr>
</tbody>
</table>
Time to onset of immune-mediated adverse events (imAEs) with IMFINZI

Median time to onset reported for select imAEs¹

- The combined safety database (N=1414) included patients treated with IMFINZI 10 mg/kg every 2 weeks¹
- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen¹

<table>
<thead>
<tr>
<th>imAE</th>
<th>All Grades n (%)</th>
<th>Days (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combined safety database (N=1414)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>32 (2.3%)</td>
<td>55.5 (24–423)</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>16 (1.1%)</td>
<td>51.5 (15–312)</td>
</tr>
<tr>
<td>Colitis or diarrhea</td>
<td>18 (1.3%)</td>
<td>73.0 (13–345)</td>
</tr>
<tr>
<td><strong>Study 1 (N=182)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>10 (5.5%)</td>
<td>42.0 (15–239)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>9 (4.9%)</td>
<td>43.0 (14–71)</td>
</tr>
</tbody>
</table>

Early recognition and treatment of imAEs observed with IMFINZI may help keep imAEs from becoming more serious¹
Management of immune-mediated adverse events

Pulmonary

Pneumonitis
Pulmonary

Immune-mediated pneumonitis¹

- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen

<table>
<thead>
<tr>
<th></th>
<th>Pneumonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades n (%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Grade 3 n (%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 4 n (%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 5 n (%)</td>
<td>1 (0.5%)</td>
</tr>
</tbody>
</table>

Signs and symptoms of pneumonitis¹

- New or worsening cough
- Shortness of breath
- Chest pain

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for signs and symptoms of pneumonitis.
Evaluate patients with suspected pneumonitis with radiographic imaging and manage as recommended below.

### Management strategies for immune-mediated pulmonary adverse events

<table>
<thead>
<tr>
<th>Definition*2</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pneumonitis</strong></td>
<td>• Asymptomatic</td>
<td>• Symptomatic</td>
<td>• Severe symptoms</td>
<td>• Life-threatening respiratory compromise</td>
</tr>
<tr>
<td></td>
<td>• Clinical or diagnostic observations only</td>
<td>• Medical intervention indicated</td>
<td>• Limiting self-care ADL†</td>
<td>• Urgent intervention indicated (eg, tracheotomy or intubation)</td>
</tr>
<tr>
<td></td>
<td>• Intervention not indicated</td>
<td>• Limiting instrumental ADL‡</td>
<td>• Oxygen indicated</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IMFINZI dose modifications</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continue treatment</strong></td>
<td><strong>Withhold IMFINZI until Grade ≤1</strong></td>
<td><strong>Permanently discontinue IMFINZI</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Steroids</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</strong></td>
<td><strong>Initial dose of 1–4 mg/kg/day prednisone or equivalent followed by a taper</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**ADL**=activities of daily living.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.

†Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

‡Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.

### Follow-up

**Worsening or no improvement:**

- Consider increasing dose of corticosteroids and/or other systemic immunosuppressants
- Withhold IMFINZI if pneumonitis worsens to Grade 2
- Permanently discontinue IMFINZI if pneumonitis worsens to Grade 3 or 4

**After withholding, IMFINZI can be resumed if:**

- Pneumonitis has improved to ≤Grade 1
- Corticosteroid dose has been reduced to <10 mg prednisone or equivalent per day

Upon improvement to <Grade 1, begin tapering corticosteroids over ≥one month.
Management of immune-mediated adverse events

Hepatic

Hepatitis
# Hepatic

## Immune-mediated hepatitis

- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen.

### Immune-mediated hepatic adverse events in Study 1 (N=182)

<table>
<thead>
<tr>
<th>Grade</th>
<th>n (%)</th>
<th>Hepatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades</td>
<td>3 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>1 (0.5%)</td>
<td></td>
</tr>
<tr>
<td>Grade 4</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Grade 5</td>
<td>1 (0.5%)</td>
<td></td>
</tr>
</tbody>
</table>

### Signs and symptoms of hepatitis

- Yellowing of skin or the whites of eyes
- Severe nausea or vomiting
- Pain on the right side of stomach area (abdomen)
- Drowsiness
- Dark urine (tea colored)
- Bleeding or bruising more easily than normal
- Feeling less hungry than usual

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for abnormal liver tests each cycle during treatment with IMFINZI.
For symptomatic immune-mediated hepatitis, manage as recommended below.

Management strategies for immune-mediated hepatic adverse events

<table>
<thead>
<tr>
<th>Definition*</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis</td>
<td>Continue treatment</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Permanently discontinue IMFINZI</td>
</tr>
<tr>
<td>IMFINZI dose modifications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
<td></td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
</tbody>
</table>

**Definition**
- Grade 1: ALT/AST ≤3x ULN or total bilirubin ≤1.5x ULN
- Grade 2: ALT/AST >3–5x ULN or total bilirubin >1.5–3x ULN
- Grade 3: ALT/AST ≤8x ULN or total bilirubin ≤5x ULN
- Grade 4: ALT/AST >8x ULN or total bilirubin >5x ULN

**Follow-up**

**Worsening or no improvement:**
- Consider increasing dose of corticosteroids and/or other systemic immunosuppressants
- Withhold IMFINZI if ALT/AST increases to >3–5x ULN or total bilirubin increases to >1.5–3x ULN
- Permanently discontinue IMFINZI if ALT/AST increases to >8x ULN or total bilirubin increases to >5x ULN

**After withholding, IMFINZI can be resumed if:**
- Hepatitis has improved to ≤Grade 1
- Corticosteroid dose has been reduced to <10 mg prednisone or equivalent per day

Upon improvement to <Grade 1, begin tapering corticosteroids over ≥one month

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
Management of immune-mediated adverse events

Gastrointestinal

Colitis
Diarrhea
**Gastrointestinal**

**Immune-mediated colitis or diarrhea\(^1\)**

- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen\(^1\)

<table>
<thead>
<tr>
<th>Immune-mediated gastrointestinal adverse events in Study 1 (N=182)(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colitis or diarrhea</strong></td>
</tr>
</tbody>
</table>
| All Grades  
  n (%)                                             |
| 23 (12.6%)                                              |
| Grade 3 or 4  
  n (%)                                           |
| 2 (1.1%)                                               |
| Grade 5  
  n (%)                                           |
| 0 (0%)                                                |

**Signs and symptoms of colitis or diarrhea\(^1\)**

- Diarrhea or more bowel movements than usual
- Stools that are black, tarry, sticky, or have blood or mucus
- Severe stomach area (abdomen) pain or tenderness

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for signs and symptoms of colitis or diarrhea.

---

\(^1\) See Important Safety Information on pages 37–38.
For symptomatic immune-mediated colitis or diarrhea, manage as recommended below

Management strategies for immune-mediated gastrointestinal adverse events

<table>
<thead>
<tr>
<th>Definition*(^2)</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diarrhea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Increase of (&lt;)4 stools/day over baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Mild increase in ostomy output vs baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Colitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Asymptomatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Clinical or diagnostic observations only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Intervention not indicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diarrhea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Increase of (4–6) stools/day over baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Moderate increase in ostomy output vs baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Colitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Abdominal pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Mucus or blood in stool</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diarrhea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Increase of (\geq 7) stools/day over baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Incontinence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Hospitalization indicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Severe increase in ostomy output vs baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Limiting self-care ADL†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Colitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Severe abdominal pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Change in bowel habits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Medical intervention indicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Peritoneal signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diarrhea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Life-threatening consequences</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Urgent intervention indicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Colitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Life-threatening consequences</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Urgent intervention indicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**IMFINZI dose modifications**

<table>
<thead>
<tr>
<th>Steroids</th>
<th>IMFINZI dose modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continue treatment</strong></td>
<td><strong>Withhold IMFINZI until Grade (\leq 1)</strong></td>
</tr>
<tr>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
</tbody>
</table>

ADL=activities of daily living.
*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
†Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.

**Follow-up****

**Worsening or no improvement:**
- Consider increasing dose of corticosteroids and/or other systemic immunosuppressants
- Withhold IMFINZI if diarrhea or colitis worsens to Grade 2
- Permanently discontinue IMFINZI if diarrhea or colitis worsens to Grade 3 or 4

**After withholding, IMFINZI can be resumed if:**
- Diarrhea or colitis has improved to \(\leq\)Grade 1
- Corticosteroid dose has been reduced to <10 mg prednisone or equivalent per day

Upon improvement to <Grade 1, begin tapering corticosteroids over ≥one month

Please see Important Safety Information on pages 37–38.
Management of immune-mediated adverse events

Endocrine

- Hypothyroidism
- Hyperthyroidism
- Adrenal insufficiency
- Hypophysitis/Hypopituitarism
- Type 1 diabetes mellitus
Endocrine

**Immune-mediated endocrinopathies¹**

- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen

### Immune-mediated endocrinopathies in Study 1 (N=182)¹

<table>
<thead>
<tr>
<th></th>
<th>Hypothyroidism</th>
<th>Hyperthyroidism</th>
<th>Adrenal insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades n (%)</td>
<td>10 (5.5%)</td>
<td>9 (4.9%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Grade 3 n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 4 n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 5 n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

- Hypophysitis/hypopituitarism and type 1 diabetes mellitus occurred in <0.1% of patients treated with IMFINZI in the combined safety database (N=1414)

### Signs and symptoms of endocrinopathies¹

- Headaches that will not go away or unusual headaches
- Extreme tiredness
- Weight gain or weight loss
- Dizziness or fainting
- Feeling more hungry or thirsty than usual
- Hair loss
- Feeling cold
- Constipation
- Voice getting deeper
- Urinating more often than usual
- Nausea or vomiting
- Stomach area (abdomen) pain
- Changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for clinical signs and symptoms of endocrinopathies. Monitor thyroid function prior to and periodically during treatment with IMFINZI. Asymptomatic patients with abnormal thyroid function tests can receive IMFINZI.
## Endocrine

For symptomatic endocrinopathies, manage as recommended below.

### Management strategies for immune-mediated hypothyroidism

<table>
<thead>
<tr>
<th>Definition*2</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
</table>
| **Hypothyroidism** | • Asymptomatic  
|              | • Clinical or diagnostic observations only  
|              | • Intervention not indicated | **Hypothyroidism** | • Symptomatic  
|              |                        | • Thyroid replacement indicated  
|              |                        | • Limiting instrumental ADL† | **Hypothyroidism** | • Severe symptoms  
|              |                        | • Limiting self-care ADL‡  
|              |                        | • Hospitalization indicated | **Hypothyroidism** | • Life-threatening consequences  
|              |                        |                          | • Urgent intervention indicated |

| IMFINZI dose modifications | Continue treatment | Continue treatment | Continue treatment |

| Clinical management | Initiate thyroid hormone replacement as clinically indicated | Initiate thyroid hormone replacement as clinically indicated | Initiate thyroid hormone replacement as clinically indicated |

ADL=activities of daily living.

* Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
† Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
‡ Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.
Endocrine

For symptomatic endocrinopathies, manage as recommended below

Management strategies for immune-mediated hyperthyroidism¹

<table>
<thead>
<tr>
<th>Definition*²</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
</table>
| Hyperthyroidism | • Asymptomatic  
• Clinical or diagnostic observations only  
• Intervention not indicated | Hyperthyroidism | • Symptomatic  
• Thyroid suppression therapy indicated  
• Limiting instrumental ADL† | Hyperthyroidism | • Severe symptoms  
• Limiting self-care ADL‡  
• Hospitalization indicated |
| Hyperthyroidism | • Severe symptoms  
• Limiting instrumental ADL† | Hyperthyroidism | • Life-threatening consequences  
• Urgent intervention indicated |

<table>
<thead>
<tr>
<th>IMFINZI dose modifications</th>
<th>Continue treatment</th>
<th>Withhold IMFINZI until clinically stable</th>
<th>Withhold IMFINZI until clinically stable</th>
<th>Symptomatic management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical management</td>
<td></td>
<td>Symptomatic management</td>
<td></td>
<td>Symptomatic management</td>
</tr>
</tbody>
</table>

ADL=activities of daily living.

* Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
† Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
‡ Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.

Follow-up¹

Worsening or no improvement:
• Symptomatic management
• Withhold IMFINZI until clinically stable if hyperthyroidism worsens to Grade 2–4

After withholding, IMFINZI can be resumed if:
• Hyperthyroidism has improved to ≤Grade 1
Endocrine

For symptomatic endocrinopathies, manage as recommended below

Management strategies for immune-mediated adrenal insufficiency and hypophysitis/hypopituitarism

<table>
<thead>
<tr>
<th>Definition*2</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal insufficiency</td>
<td>Asymptomatic</td>
<td>Clinical or diagnostic observations only</td>
<td>Intervention not indicated</td>
<td></td>
</tr>
<tr>
<td>Hypophysitis/Hypopituitarism†</td>
<td>Asymptomatic or mild symptoms</td>
<td>Clinical or diagnostic observations only</td>
<td>Intervention not indicated</td>
<td></td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>Moderate symptoms</td>
<td>Medical intervention indicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysitis/Hypopituitarism†</td>
<td>Moderate</td>
<td>Minimal, local, or noninvasive intervention indicated</td>
<td>Limiting age-appropriate instrumental ADL‡</td>
<td></td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>Severe symptoms</td>
<td>Hospitalization indicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysitis/Hypopituitarism†</td>
<td>Severe or medically significant, but not immediately life threatening</td>
<td>Hospitalization or prolongation of existing hospitalization indicated</td>
<td>Disabling</td>
<td>Limiting self-care ADL§</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>Life-threatening consequences</td>
<td>Urgent intervention indicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysitis/Hypopituitarism†</td>
<td>Life-threatening consequences</td>
<td>Urgent intervention indicated</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IMFINZI dose modifications

- Continue treatment
- Withhold IMFINZI until clinically stable
- Withhold IMFINZI until clinically stable

Clinical management

- Initiate 1–2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
- Initiate 1–2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated

Follow-up†

Worsening or no improvement:
- Consider increasing dose of corticosteroids and/or other systemic immunosuppressants
- Withhold IMFINZI until clinically stable if endocrinopathies worsen to Grade 2–4

After withholding, IMFINZI can be resumed if:
- Endocrinopathies have improved to ≤Grade 1
- Corticosteroid dose has been reduced to <10 mg prednisone or equivalent per day

Upon improvement to <Grade 1, begin tapering corticosteroids over ≥one month

---

*ADL=activities of daily living.
†Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
‡Grade definition for endocrine disorders—other.
\(\dagger\) Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
§Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.

---

Please see Important Safety Information on pages 37–38.
**Endocrine**

For symptomatic endocrinopathies, manage as recommended below

Management strategies for type 1 diabetes mellitus

<table>
<thead>
<tr>
<th>Definition*</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 diabetes mellitus (hyperglycemia)</td>
<td>Fasting glucose value &gt;ULN –160 mg/dL</td>
<td>Fasting glucose value &gt;160–250 mg/dL</td>
<td>&gt;250–500 mg/dL</td>
<td>&gt;500 mg/dL</td>
</tr>
<tr>
<td>Type 1 diabetes mellitus (hyperglycemia)</td>
<td>Fasting glucose value &gt;8.9 mmol/L</td>
<td>&gt;8.9–13.9 mmol/L</td>
<td>&gt;13.9–27.8 mmol/L</td>
<td>&gt;27.8 mmol/L</td>
</tr>
</tbody>
</table>

**IMFINZI dose modifications**
- Continue treatment
- Withhold IMFINZI until clinically stable
- Withhold IMFINZI until clinically stable

**Clinical management**
- Initiate treatment with insulin as clinically indicated
- Initiate treatment with insulin as clinically indicated

ULN = upper limit of normal.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.

**Follow-up’**

**Worsening or no improvement:**
- Initiate treatment with insulin as clinically indicated
- Withhold IMFINZI until clinically stable if type 1 diabetes mellitus worsens to Grade 2–4

**After withholding, IMFINZI can be resumed if:**
- Type 1 diabetes mellitus has improved to ≤Grade 1
Management of immune-mediated adverse events

Renal

Nephritis
Renal

Immune-mediated nephritis

- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen

<table>
<thead>
<tr>
<th>Immune-mediated renal adverse events in Study 1 (N=182)</th>
</tr>
</thead>
</table>
| All Grades  
n (%) | Nephritis |
| Grade 3  
n (%) | 0 (0%) |
| Grade 4  
n (%) | 0 (0%) |
| Grade 5  
n (%) | 0 (0%) |

Signs and symptoms of nephritis

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

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for abnormal renal function tests prior to and during each cycle during treatment with IMFINZI.
Renal

For symptomatic immune-mediated nephritis, manage as recommended below

Management strategies for immune-mediated renal adverse events

<table>
<thead>
<tr>
<th>Definition*2</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephritis†</td>
<td>Asymptomatic or mild symptoms</td>
<td>Nephritis†</td>
<td>Moderate, local, or noninvasive intervention indicated</td>
<td>Nephritis†</td>
</tr>
<tr>
<td></td>
<td>Clinical or diagnostic observations only</td>
<td></td>
<td>Limiting instrumental ADL‡</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention not indicated</td>
<td>With creatinine</td>
<td>With creatinine</td>
<td>With creatinine</td>
</tr>
<tr>
<td></td>
<td>≤1.5x ULN</td>
<td>&gt;1.5–3x ULN</td>
<td>&gt;3–6x ULN</td>
<td>&gt;6x ULN</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IMFINZI dose modifications</th>
<th>Continue treatment</th>
<th>Withhold IMFINZI until Grade ≤1</th>
<th>Permanently discontinue IMFINZI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
<td></td>
</tr>
</tbody>
</table>

**IMFINZI** dose

Continue treatment | Withhold treatment | Permanently discontinue treatment

Follow-up†

Worsening or no improvement:
- Consider increasing dose of corticosteroids and/or other systemic immunosuppressants
- Withhold IMFINZI if serum creatinine increases to >1.5–3x ULN
- Permanently discontinue IMFINZI if serum creatinine increases to >3x ULN

After withholding, IMFINZI can be resumed if:
- Nephritis and serum creatinine have improved to ≤Grade 1
- Corticosteroid dose has been reduced to <10 mg prednisone or equivalent per day

Upon improvement to <Grade 1, begin tapering corticosteroids over ≥one month

ULN=upper limit of normal; ADL=activities of daily living.
*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
†Grade definition for renal and urinary disorders—other.
‡Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
§Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.
Management of immune-mediated adverse events

Skin

Rash
Dermatitis
Skin

Immune-mediated rash or dermatitis

- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen

<table>
<thead>
<tr>
<th>Immune-mediated skin adverse events in Study 1 (N=182)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rash or dermatitis</strong></td>
</tr>
<tr>
<td><strong>All Grades</strong></td>
</tr>
<tr>
<td>n (%)</td>
</tr>
<tr>
<td>20 (11.0%)</td>
</tr>
<tr>
<td><strong>Grade 3</strong></td>
</tr>
<tr>
<td>n (%)</td>
</tr>
<tr>
<td>1 (0.5%)</td>
</tr>
<tr>
<td><strong>Grade 4</strong></td>
</tr>
<tr>
<td>n (%)</td>
</tr>
<tr>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Grade 5</strong></td>
</tr>
<tr>
<td>n (%)</td>
</tr>
<tr>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Signs and symptoms of rash or dermatitis

- Rash
- Itching
- Skin blistering

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for signs and symptoms of rash or dermatitis.
## Skin

For symptomatic immune-mediated rash or dermatitis, manage as recommended below.

### Management strategies for immune-mediated skin adverse events

<table>
<thead>
<tr>
<th>Definition*2</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash or dermatitis</td>
<td>• Covering &lt;10% BSA</td>
<td>Rash or dermatitis</td>
<td>• Covering 10%–30% BSA</td>
<td>Rash or dermatitis</td>
</tr>
<tr>
<td>Rash or dermatitis</td>
<td>• Covering &gt;30% BSA</td>
<td>Rash or dermatitis</td>
<td>• Covering &gt;30% BSA</td>
<td></td>
</tr>
<tr>
<td>Rash or dermatitis</td>
<td>• Life-threatening consequences</td>
<td>Rash or dermatitis</td>
<td>• Urgent intervention needed</td>
<td></td>
</tr>
</tbody>
</table>

**IMFINZI dose modifications**
- Continue treatment
- If Grade 2 for >1 week, withhold IMFINZI until Grade ≤1
- Withhold IMFINZI until Grade ≤1
- Permanently discontinue IMFINZI

**Steroids**
- Consider initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper
- Consider initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper

**Follow-up**

**Worsening or no improvement:**
- Consider increasing dose of corticosteroids and/or other systemic immunosuppressants
- Withhold IMFINZI if rash or dermatitis remains at Grade 2 for >1 week or worsens to Grade 3
- Permanently discontinue IMFINZI if rash or dermatitis worsens to Grade 4

**After withholding, IMFINZI can be resumed if:**
- Rash or dermatitis has improved to ≤Grade 1
- Corticosteroid dose has been reduced to <10 mg prednisone or equivalent per day

Upon improvement to <Grade 1, begin tapering corticosteroids over ≥one month

---

BSA = body surface area.

* Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
Management of immune-mediated adverse events

Infection
Infection

The Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen:

Infection in Study 1 (N=182)

<table>
<thead>
<tr>
<th></th>
<th>Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades n (%)</td>
<td>54 (29.7%)</td>
</tr>
<tr>
<td>Grade 3 or 4 n (%)</td>
<td>11 (6.0%)</td>
</tr>
</tbody>
</table>

Five (2.7%) patients were experiencing infection at the time of death:

Urinary tract infections were the most common cause of Grade 3 or higher infection, occurring in 8 (4.4%) patients:

Signs and symptoms of infection

- Fever
- Cough
- Frequent urination
- Pain when urinating
- Flu-like symptoms

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for signs and symptoms of infection and treat with anti-infectives for suspected or confirmed infections.
Infection

For symptomatic infection, manage as recommended below

Management strategies for infection

<table>
<thead>
<tr>
<th>Definition*2</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| • Asymptomatic or mild symptoms
• Clinical or diagnostic observations only
• Intervention not indicated |
| Infection    |         |         |         |         |
| • Moderate
• Minimal, local, or noninvasive intervention indicated
• Limiting age-appropriate instrumental ADL† |
| Infection    |         |         |         |         |
| • Severe or medically significant but not immediately life threatening
• Hospitalization or prolongation of existing hospitalization indicated
• Disabling
• Limiting self-care ADL‡ |
| Infection    |         |         |         |         |
| • Life-threatening consequences
• Urgent intervention indicated |

IMFINZI dose modifications

- May continue treatment with IMFINZI§
- May continue treatment with IMFINZI§
- Withhold IMFINZI until Grade ≤1

Clinical management

- Symptomatic management; treat with anti-infectives for suspected or confirmed infections
- Symptomatic management; treat with anti-infectives for suspected or confirmed infections
- Symptomatic management; treat with anti-infectives for suspected or confirmed infections

ADL=activities of daily living.
* Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.
† Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
‡ Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.
§ Based on clinical judgment.

Follow-up

Worsening or no improvement:
- Treat with anti-infectives for suspected or confirmed infections
- Withhold IMFINZI until clinically stable if infection worsens to Grade 3 or 4

After withholding, IMFINZI can be resumed if:
- Infection has improved to ≤Grade 1
Management of immune-mediated adverse events

Infusion-related reactions
Infusion-related reactions

- Study 1 safety data reflect exposure to IMFINZI in 182 patients with locally advanced or metastatic urothelial carcinoma in whom disease has progressed during or after one standard platinum-based regimen.

<table>
<thead>
<tr>
<th>Infusion-related reactions in Study 1 (N=182)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades</td>
</tr>
<tr>
<td>n (%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infusion-related reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 (1.6%)</td>
</tr>
</tbody>
</table>

**Signs and symptoms of infusion-related reactions**

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

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Monitor patients for signs and symptoms of an infusion-related reaction.
### Infusion-related reactions

For symptomatic infusion-related reactions, manage as recommended below.

#### Management strategies for infusion-related reactions

**Definition**

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infusion-related reactions</strong></td>
<td><strong>Infusion-related reactions</strong></td>
<td><strong>Infusion-related reactions</strong></td>
<td><strong>Infusion-related reactions</strong></td>
</tr>
<tr>
<td>- Mild transient reaction</td>
<td>- Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDs, narcotics, IV fluids)</td>
<td>- Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion)</td>
<td>- Life-threatening consequences</td>
</tr>
<tr>
<td>- Infusion interruption not indicated</td>
<td>- Prophylactic medications indicated for ≤24 hr</td>
<td>- Recurrence of symptoms following initial improvement</td>
<td>- Urgent intervention indicated</td>
</tr>
<tr>
<td>- Intervention not indicated</td>
<td></td>
<td>- Hospitalization indicated for clinical sequelae</td>
<td></td>
</tr>
</tbody>
</table>

**IMFINZI dose modifications**

<table>
<thead>
<tr>
<th>IMFINZI dose modifications</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interrupt or slow the rate of infusion</strong></td>
<td><strong>Interrupt or slow the rate of infusion</strong></td>
<td><strong>Permanently discontinue IMFINZI</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Clinical management**

<table>
<thead>
<tr>
<th>IMFINZI dose modifications</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consider pre-medications with subsequent doses</strong></td>
<td><strong>Consider pre-medications with subsequent doses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NSAIDs = nonsteroidal anti-inflammatory drugs; IV = intravenous.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.

---

**Follow-up**

**Worsening or no improvement:**
- Interrupt or slow the rate of infusion
- Permanently discontinue IMFINZI if infusion-related reaction worsens to Grade 3 or 4
Management of immune-mediated adverse events

Other
Other

Monitor patients for the following signs and symptoms of other immune-mediated adverse events (imAEs)\(^1\)

- Neck stiffness
- Headache
- Confusion
- Fever
- Changes in mood or behavior
- Blurry vision, double vision, or other vision problems
- Eye pain or redness

For suspected imAEs, perform adequate evaluation to confirm etiology or exclude alternate etiologies.

Management strategies for other imAEs\(^1\)

<table>
<thead>
<tr>
<th>IMFINZI dose modifications</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>May continue treatment with IMFINZI*</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Permanently discontinue IMFINZI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical management</td>
<td>Symptomatic management(^1)</td>
<td>Symptomatic management(^1)</td>
<td>Consider initial dose of 1–4 mg/kg/day prednisone or equivalent followed by taper</td>
<td></td>
</tr>
</tbody>
</table>

*Based on clinical judgment.  
†Administer corticosteroids as appropriate.

Follow-up\(^1\)

**Worsening or no improvement:**
- Consider increasing dose of corticosteroids and/or other systemic immunosuppressants
- Withhold IMFINZI until clinically stable if imAE worsens to Grade 3
- Permanently discontinue IMFINZI if imAE worsens to Grade 4

**After withholding, IMFINZI can be resumed if:**
- imAE has improved to ≤Grade 1
- Corticosteroid dose has been reduced to <10 mg prednisone or equivalent per day

Upon improvement to <Grade 1, begin tapering corticosteroids over ≥one month
Summary

Grade 2–4 immune-mediated adverse event (imAE) management and dosing modifications

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Severity</th>
<th>Dosing modification IMFINZI</th>
<th>Initial steroid treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary</strong> • Pneumonitis</td>
<td>Grade 2</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td></td>
<td>Grade 3 or 4</td>
<td>Permanently discontinue IMFINZI</td>
<td>Initial dose of 1–4 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td><strong>Hepatic</strong> • Hepatitis</td>
<td>Grade 2</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td></td>
<td>Grade 3 with ALT/AST ≤8x ULN or total bilirubin ≤5x ULN</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 3 with ALT/AST &gt;8x ULN or total bilirubin &gt;5x ULN</td>
<td>Permanently discontinue IMFINZI</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong> • Colitis • Diarrhea</td>
<td>Grade 2</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td></td>
<td>Grade 3 or 4</td>
<td>Permanently discontinue IMFINZI</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td><strong>Endocrine</strong> • Hypothyroidism</td>
<td>Grade 2–4</td>
<td>Continue treatment with IMFINZI</td>
<td>Initiate thyroid hormone replacement as clinically indicated</td>
</tr>
<tr>
<td><strong>Endocrine</strong> • Hyperthyroidism</td>
<td>Grade 2–4</td>
<td>Withhold IMFINZI until clinically stable</td>
<td>Symptomatic management</td>
</tr>
</tbody>
</table>

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

For patients with Grade 1 imAEs, continue current treatment and monitor closely for symptom worsening

- Withheld IMFINZI may be resumed when adverse events resolve to Grade ≤1
- Upon symptom improvement, gradually taper corticosteroids over ≥one month

Please see Important Safety Information on pages 37–38.
# Grade 2–4 imAE management and dosing modifications (continued)¹

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Severity</th>
<th>Dosing modification</th>
<th>Initial steroid treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endocrine</strong></td>
<td>Grade 2–4</td>
<td>Withhold IMFINZI until clinically stable</td>
<td>Initiate 1–2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated</td>
</tr>
<tr>
<td>• Adrenal insufficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hypophysitis/Hypopituitarism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endocrine</strong></td>
<td>Grade 2–4</td>
<td>Withhold IMFINZI until clinically stable</td>
<td>Initiate treatment with insulin as clinically indicated</td>
</tr>
<tr>
<td>• Type 1 diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td>Grade 2 with creatinine &gt;1.5–3x ULN</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td>• Nephritis</td>
<td>Grade 3 with creatinine &gt;3–6x ULN</td>
<td>Permanently discontinue IMFINZI</td>
<td>Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td></td>
<td>Grade 4 with creatinine &gt;6x ULN</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>Grade 2 for &gt;1 week</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Consider initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td>• Rash</td>
<td>Grade 3</td>
<td>Permanently discontinue IMFINZI</td>
<td></td>
</tr>
<tr>
<td>• Dermatitis</td>
<td>Grade 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>Grade 2</td>
<td>May continue treatment with IMFINZI*</td>
<td>Symptomatic management; treat with anti-infectives for suspected or confirmed infections</td>
</tr>
<tr>
<td></td>
<td>Grade 3 or 4</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Symptomatic management; treat with anti-infectives for suspected or confirmed infections</td>
</tr>
<tr>
<td><strong>Infusion-related reactions</strong></td>
<td>Grade 1 or 2</td>
<td>Interrupt or slow the rate of infusion</td>
<td>Consider pre-medications with subsequent doses</td>
</tr>
<tr>
<td></td>
<td>Grade 3 or 4</td>
<td>Permanently discontinue IMFINZI</td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Grade 2</td>
<td>May continue treatment with IMFINZI*</td>
<td>Symptomatic management†</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>Withhold IMFINZI until Grade ≤1</td>
<td>Symptomatic management†</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Permanently discontinue IMFINZI</td>
<td>Consider initial dose of 1–4 mg/kg/day prednisone or equivalent followed by taper</td>
</tr>
</tbody>
</table>

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

*Based on clinical judgment.
†Administer corticosteroids as appropriate.

- Withheld IMFINZI may be resumed when adverse events resolve to Grade ≤1¹
- Upon symptom improvement, gradually taper corticosteroids over ≥one month¹
Important Safety Information

There are no contraindications for IMFINZI™ (durvalumab).

Monitor patients for clinical signs and symptoms of immune-mediated pneumonitis, hepatitis, colitis or diarrhea, endocrinopathies, nephritis, rash or dermatitis, and other immune-mediated adverse reactions. Please refer to the full Prescribing Information for important dose management information specific to adverse reactions.

Immune-Mediated Pneumonitis
In the combined safety database (n=1414), immune-mediated pneumonitis occurred in 32 patients (2.3%), including 1 fatal case (0.1%) and 6 Grade 3–4 cases (0.4%). In Study 1 (n=182), 1 patient (0.5%) died from immune-mediated pneumonitis. Monitor patients for signs and symptoms of pneumonitis and evaluate with radiographic imaging when suspected. Administer corticosteroids for ≥Grade 2 pneumonitis. Withhold IMFINZI for Grade 2 pneumonitis; permanently discontinue for Grade 3–4 pneumonitis.

Immune-Mediated Hepatitis
In the combined safety database (n=1414), immune-mediated hepatitis occurred in 16 patients (1.1%), including 1 fatal case (<0.1%) and 9 Grade 3 cases (0.6%). Grade 3–4 elevations in ALT occurred in 40/1342 patients (3.0%), AST in 58/1336 patients (4.3%), and total bilirubin in 37/1341 patients (2.8%). In Study 1 (n=182), 1 patient (0.5%) died from immune-mediated hepatitis, and 2 patients (1.1%) experienced immune-mediated hepatitis, including 1 Grade 3 case (0.5%). Monitor patients for abnormal liver tests in each cycle during treatment with IMFINZI. Administer corticosteroids and withhold IMFINZI for Grade 2–3 ALT or AST >3–5X ULN or ≤8X ULN or total bilirubin >1.5–3X ULN or ≤5X ULN. Permanently discontinue IMFINZI in patients with Grade 3 ALT or AST >8X ULN or total bilirubin >5X ULN, or in patients with concurrent ALT or AST >3X ULN and total bilirubin >2X ULN with no other cause.

Immune-Mediated Colitis
In the combined safety database (n=1414), immune-mediated colitis or diarrhea occurred in 18 patients (1.3%), including 1 Grade 4 case (<0.1%) and 4 Grade 3 cases (0.3%). In Study 1 (n=182), 23 patients (12.6%) experienced colitis or diarrhea, including 2 Grade 3–4 cases (1.1%). Monitor patients for signs and symptoms of colitis or diarrhea. Administer corticosteroids for ≥Grade 2 colitis or diarrhea. Withhold IMFINZI for Grade 2 colitis or diarrhea; permanently discontinue for Grade 3–4 colitis or diarrhea.

Immune-Mediated Endocrinopathies
• Immune-mediated thyroid disorders, adrenal insufficiency, type 1 diabetes mellitus and hypophysitis/hypopituitarism have occurred with IMFINZI. Monitor patients for clinical signs and symptoms of endocrinopathies. For Grade 2–4 endocrinopathies (except hypothyroidism) withhold dose until clinically stable and offer symptomatic management for hyperthyroidism. For Grade 2–4 hypothyroidism, initiate thyroid hormone replacement as needed
• Immune-mediated hypothyroidism and hyperthyroidism—In the combined safety database (n=1414), immune-mediated hypothyroidism and hyperthyroidism occurred in 136 patients (9.6%) and 81 patients (5.7%), respectively. Thyroiditis occurred in 10 patients (0.7%), including 1 Grade 3 case (<0.1%) in a patient who had a myocardial infarction. In 9 patients with thyroiditis, transient hyperthyroidism preceded hypothyroidism. In Study 1 (n=182), Grade 1–2 hypothyroidism or thyroiditis occurred in 10 patients (5.5%). Grade 1–2 hyperthyroidism or thyroiditis leading to hyperthyroidism occurred in 9 patients (4.9%). Monitor patients for abnormal thyroid function tests prior to and periodically during treatment
• Immune-mediated adrenal insufficiency—In the combined safety database (n=1414), immune-mediated adrenal insufficiency occurred in 13 patients (0.9%), including 2 Grade 3 cases (0.1%). In Study 1 (n=182), Grade 1 adrenal insufficiency occurred in 1 patient (0.5%). Administer corticosteroids and hormone replacement as clinically indicated
• Type 1 diabetes mellitus—In the combined safety database (n=1414), new onset type 1 diabetes mellitus without an alternative etiology occurred in 1 patient (<0.1%). For type 1 diabetes mellitus, initiate insulin as indicated and withhold IMFINZI until clinically stable
• Hypophysitis—In the combined safety database (n=1414), hypopituitarism leading to adrenal insufficiency and diabetes insipidus occurred in 1 patient (<0.1%). Administer corticosteroids and hormone replacement as clinically indicated
Important Safety Information (continued)

Other Immune-Mediated Adverse Reactions

- IMFINZI has caused immune-mediated rash. Other immune-related adverse reactions, including aseptic meningitis, hemolytic anemia, immune thrombocytopenic purpura, myocardiitis, myositis, nephritis, and ocular inflammatory toxicity including uveitis and keratitis, have occurred in ≤1.0% of patients treated with IMFINZI.

- Immune-mediated rash or dermatitis—In the combined safety database (n=1414), immune-mediated rash or dermatitis occurred in 220 patients (15.6%) and 4 patients (0.3%) developed vitiligo. In Study 1 (n=182), 20 patients (11.0%) developed rash, including 1 Grade 3 case (0.5%). Patients should be monitored for signs and symptoms of rash or dermatitis. Administer corticosteroids if indicated. Withhold IMFINZI for Grade 3 rash or dermatitis or Grade 2 rash or dermatitis lasting >1 week. Permanently discontinue IMFINZI in patients with Grade 4 rash or dermatitis.

- Immune thrombocytopenic purpura—In the combined safety database (n=1414), 1 fatal case (<0.1%) of immune thrombocytopenic purpura occurred. Monitor patients for signs and symptoms of immune thrombocytopenic purpura.

- Nephritis—In the combined safety database (n=1414), immune-mediated nephritis occurred in 3 patients (0.2%), including 2 Grade 3 cases (0.1%). Monitor patients for abnormal renal function tests prior to and during each cycle of IMFINZI. Administer corticosteroids for ≥Grade 2 nephritis (creatinine >1.5X ULN). Withhold IMFINZI for Grade 2 nephritis; permanently discontinue for ≥Grade 3 nephritis (creatinine >3X ULN).

Infection

Severe infections, including sepsis, necrotizing fasciitis, and osteomyelitis, occurred in patients receiving IMFINZI. In the combined safety database (n=1414), infections occurred in 531 patients (37.6%). In Study 1 (n=182), infections occurred in 54 patients (29.7%). 11 patients (6.0%) experienced Grade 3–4 infection and 5 patients (2.7%) were experiencing infection at the time of death. 8 patients (4.4%) experienced urinary tract infection, the most common ≥Grade 2 infection. Monitor patients for signs and symptoms of infection and treat with anti-infectives for suspected or confirmed infections. Withhold IMFINZI for ≥Grade 3 infection.

Infusion-Related Reactions

In the combined safety database (n=1414), severe infusion-related reactions occurred in 26 patients (1.8%). In Study 1 (n=182), infusion-related reactions occurred in 3 patients (1.6%). There were 5 Grade 3 (0.4%) and no Grade 4 or 5 reactions. Patients should be monitored for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1–2 infusion-related reactions and permanently discontinue for Grade 3–4 infusion-related reactions.

Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. There are no data on the use of IMFINZI in pregnant women. Advise pregnant women of the potential risk to a fetus and advise women of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of IMFINZI.

Nursing Mothers

There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for adverse reactions in breastfed infants from IMFINZI, advise a lactating woman not to breastfeed during treatment and for at least 3 months after the last dose.

Most Common Adverse Reactions

- The most common adverse reactions (≥15%) were fatigue (39%), musculoskeletal pain (24%), constipation (21%), decreased appetite (19%), nausea (16%), peripheral edema (15%), and urinary tract infection (15%). The most common Grade 3 or 4 adverse reactions (≥3%) were fatigue, urinary tract infection, musculoskeletal pain, abdominal pain, dehydration, and general physical health deterioration.

- Adverse reactions leading to discontinuation of IMFINZI occurred in 3.3% of patients. Serious adverse reactions occurred in 46% of patients. The most frequent serious adverse reactions (≥2%) were acute kidney injury (4.9%), urinary tract infection (4.4%), musculoskeletal pain (4.4%), liver injury (3.3%), general physical health deterioration (3.3%), sepsis, abdominal pain, and pyrexia/tumor associated fever (2.7% each).

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

Please see complete Prescribing Information including Patient Information at AZPICentral.com.
Lighthouse: A personal approach to supporting your patients’ experience with IMFINZI

Lighthouse is a program that provides your patients with constant support during their IMFINZI treatment, encouraging them to monitor their overall experience, including tracking any side effects that they may have.

Lighthouse offers patients:
• **24/7 support** from medically trained professionals, called Advocates
• Tools to help them track their symptoms
• Education on the importance of monitoring

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### How Lighthouse Can Help

- **Encourage patients to track, monitor, and report imAEs**
- **Bridge communication between you and your patients**
- **Enable you and your practice to stay informed**

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For more information about Lighthouse and to encourage your patients to sign up:

VISIT LighthouseProgram.com/Join  |  CALL 1-855-546-8731
Help your patients get the resources they need

Financial assistance:

AstraZeneca Access 360™ provides patient access, reimbursement support, and information about affordability programs for AstraZeneca’s medicines.

Our program helps patients and providers with:

• Identifying and understanding prescription coverage, out-of-pocket costs, and pharmacy options
• Prior authorization support
• Reimbursement process

Access 360 is staffed with knowledgeable AstraZeneca Reimbursement Counselors who are available at 844-ASK-A360 (844-275-2360) Monday–Friday 8 AM–8 PM ET. For additional information, visit www.MyAccess360.com.

Additional support materials:

Visit www.IMFINZI.com to download these and other materials to support your patients on IMFINZI.

Lighthouse Patient Brochure
This brochure helps patients better understand their treatment

IMFINZI Guide to Monitoring Side Effects
Explains why monitoring is important and what to look out for

Daily Side Effect Tracker
A simple tool to help patients track signs of side effects

Immunotherapy Wallet Card
This card is a way for patients to alert ER staff of their current treatment

Please see Important Safety Information on pages 37–38.
AstraZeneca offers a range of services for your patients’ needs

Immune-mediated Adverse Event (imAE) Reminder Sheet
• Use the reminder sheet to help monitor your patients’ imAEs. Go to IMFINZI.com/hcp/resources

IMFINZI.com/hcp
• Learn more about IMFINZI and download additional resources

AstraZeneca Information Center (AZIC) at 1-800-236-9933
• Call to receive additional information about AstraZeneca products

Oncology Nurse Educators
• Connect with an Oncology Nurse Educator to receive live patient education and training

Please see Important Safety Information on pages 37–38.