PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

IMFINZI®
durvalumab for injection
Intravenous Infusion, 50 mg durvalumab / mL
120 mg and 500 mg single-use vials
Antineoplastic agent, monoclonal antibody

IMFINZI (durvalumab) has been issued marketing authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for IMFINZI, please refer to Health Canada’s Notice of Compliance with conditions - drug products web site: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/index-eng.php.

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

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Submission Control No: 202953

Date of Approval: NOV 3, 2017
What is a Notice of Compliance with Conditions (NOC/c)?

An NOC/c is a form of market approval granted to a product on the basis of promising evidence of clinical effectiveness following review of the submission by Health Canada.

Products authorized under Health Canada’s NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

What will be different about this Product Monograph?

The following Product Monograph will contain boxed text at the beginning of each major section clearly stating the nature of the market authorization. Sections for which NOC/c status holds particular significance will be identified in the left margin by the symbol NOC/c. These sections may include, but are not limited to, the following:

- Indications;
- Action and Clinical Pharmacology;
- Warnings and Precautions;
- Adverse Reactions;
- Dosage and Administration; and
- Clinical Trials.

Adverse Drug Reaction Reporting and Re-Issuance of the Product Monograph

Health care providers are encouraged to report Adverse Drug Reactions associated with normal use of these and all drug products to Health Canada’s Canada Vigilance Program at 1-866-234-2345. The Product Monograph will be re-issued in the event of serious safety concerns previously unidentified or at such time as the sponsor provides the additional data in support of the product’s clinical benefit. Once the latter has occurred, and in accordance with the NOC/c policy, the conditions associated with market authorization will be removed.
RECENT MAJOR LABEL CHANGES

Not Applicable.

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Urothelial Carcinoma

IMFINZI (durvalumab) 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

Marketing authorization with conditions was based on a promising tumour response rate and durability of response. An improvement in survival or disease-related symptoms has not been established (see CLINICAL TRIALS).

1.1 Pediatrics

Pediatrics (<18 years of age): The safety and efficacy of IMFINZI in patients younger than 18 years of age have not been established.

1.2 Geriatrics

Geriatrics (> 65 years of age): No overall differences in safety or efficacy were reported between elderly patients (≥ 65 years of age) and younger patients (<65 years of age) (see WARNINGS AND PRECAUTIONS, Geriatrics).

2 CONTRAINDICATIONS

IMFINZI (durvalumab) is contraindicated in patients who are hypersensitive to durvalumab or to any ingredient in the formulation or component of the container. For a complete listing of ingredients, see DOSAGE FORMS, STRENGTHS, COMPOSITION and PACKAGING section of the Product Monograph.
3 DOSAGE AND ADMINISTRATION

3.1 Recommended Dose and Dosage Adjustment

Urothelial Carcinoma

Recommended Dose

The recommended dose of IMFINZI (durvalumab) is 10 mg/kg administered as an intravenous infusion over 60 minutes every 2 weeks as long as clinical benefit is observed or until unacceptable toxicity.

For previously treated patients in the pivotal study, treatment with IMFINZI was permitted until one or more criteria for discontinuation were met including:

- Adverse event (AE) experienced that contraindicates further dosing
- Pregnancy or intent to become pregnant
- Any AE that met criteria for discontinuation
- AE related to drug that is Grade ≥ 3, with the exception of toxicities that did not meet criteria for discontinuation
- Grade ≥ 3 infusion reaction
- Confirmation of progressive disease and investigator determination that the patient no longer benefited from treatment

Dosage Adjustment

Dose escalation or reduction is not recommended. Dose withholding or discontinuation may be required based on individual safety and tolerability. Guidelines for management of immune-mediated adverse reactions are described in Table 1. Refer to WARNINGS AND PRECAUTIONS for further monitoring and evaluation information.

Table 1 Recommended Treatment Modifications for IMFINZI

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Severitya</th>
<th>IMFINZI Treatment Modification</th>
<th>Corticosteroid Treatment Unless Otherwise Specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune-mediated pneumonitis</td>
<td>Grade 2</td>
<td>Withhold doseb</td>
<td>Initiate 1 to 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</td>
<td>Initiate 1 to 4 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td>Immune-mediated hepatitis</td>
<td>Grade 2 with ALT or AST &gt;3-5xULN and/or total bilirubin &gt;1.5-3xULN</td>
<td>Withhold doseb</td>
<td>Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td>Adverse Reactions</td>
<td>Severity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>IMFINZI Treatment Modification</td>
<td>Corticosteroid Treatment Unless Otherwise Specified</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>--------------------------------</td>
<td>----------------------------------------------------</td>
</tr>
<tr>
<td>Grade 3 with AST or ALT ≤8xULN or total bilirubin ≤5xULN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 with AST or ALT &gt;8xULN or total bilirubin &gt;5xULN</td>
<td></td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Concurrent ALT or AST &gt;3xULN and total bilirubin &gt;2xULN with no other cause</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immune-mediated colitis or diarrhea</td>
<td>Grade 2</td>
<td>Withhold dose&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Initiate 1 to 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</td>
<td></td>
</tr>
<tr>
<td>Immune-mediated endocrinopathies: Hyperthyroidism</td>
<td>Grade 2-4</td>
<td>Withhold dose until clinically stable</td>
<td>Symptomatic management</td>
</tr>
<tr>
<td>Immune-mediated endocrinopathies: Hypothyroidism</td>
<td>Grade 2-4</td>
<td>No change</td>
<td>Initiate thyroid hormone replacement as clinically indicated</td>
</tr>
<tr>
<td>Immune-mediated endocrinopathies: Adrenal insufficiency, Hypophysitis/ Hypopituitarism</td>
<td>Grade 2-4</td>
<td>Withhold dose until clinically stable</td>
<td>Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated</td>
</tr>
<tr>
<td>Immune-mediated endocrinopathies: Type 1 diabetes mellitus</td>
<td>Grade 2-4</td>
<td>Withhold dose until clinically stable</td>
<td>Initiate treatment with insulin as clinically indicated</td>
</tr>
<tr>
<td>Adverse Reactions</td>
<td>Severitya</td>
<td>IMFINZI Treatment Modification</td>
<td>Corticosteroid Treatment Unless Otherwise Specified</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>----------------------------------</td>
<td>--------------------------------</td>
<td>---------------------------------------------------</td>
</tr>
<tr>
<td>Immune-mediated nephritis</td>
<td>Grade 2 with serum creatinine &gt;1.5-3x (ULN or baseline)</td>
<td>Withhold doseb</td>
<td>Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td></td>
<td>Grade 3 with serum creatinine &gt;3x baseline or &gt;3-6xULN; Grade 4 with serum creatinine &gt;6xULN</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Immune-mediated rash or dermatitis</td>
<td>Grade 2 for &gt;1 week</td>
<td>Withhold doseb</td>
<td>Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>Grade 3 or 4</td>
<td>Withhold dose</td>
<td>Symptomatic management; treat with anti-infectives for suspected or confirmed infections</td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>Grade 1 or 2</td>
<td>Interrupt or slow the rate of infusionc</td>
<td>May consider pre-medications for prophylaxis of subsequent infusion reactions</td>
</tr>
<tr>
<td></td>
<td>Grade 3 or 4</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
<tr>
<td>Other immune-mediated adverse reactions</td>
<td>Grade 3</td>
<td>Withhold doseb</td>
<td>Consider initial dose of 1 mg/kg/day to 4 mg/kg/day prednisone or equivalent followed by taper</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Permanently discontinue</td>
<td></td>
</tr>
</tbody>
</table>

a Common Terminology Criteria for Adverse Events, version 4.03. ALT: alanine aminotransferase; AST: aspartate aminotransferase; ULN: upper limit of normal.

b Based on severity of the adverse reactions, IMFINZI should be withheld and corticosteroids administered. Consider increasing dose of corticosteroids and/or using other systemic immunosuppressants (see Table 1) if there is worsening or no improvement. Upon improvement to ≤Grade 1, corticosteroid taper should be initiated and continued over at least 1 month. IMFINZI can be resumed if the adverse reactions improved to ≤Grade 1 and the corticosteroid dose has been reduced to ≤10 mg prednisone or equivalent per day.

c In case of infusion-related reactions, infusion rate of IMFINZI may be decreased by 50% or be temporarily interrupted until resolution of event.
Special Populations

A population pharmacokinetic (PK) analysis, could not detect any effect on the clearance (CL) parameter in the model due to patient age, body weight, gender and race, therefore no dose adjustment of IMFINZI is recommended (see ACTION AND CLINICAL PHARMACOLOGY).

Pediatrics (<18 years of age): The safety and efficacy of IMFINZI in patients younger than 18 years of age have not been established.

Geriatrics (≥65 years of age): No dose adjustment is recommended for elderly patients (≥65 years of age) (see ACTION AND CLINICAL PHARMACOLOGY).

Renal Impairment: A population PK analysis could not detect any effect of mild to moderate renal impairment on the CL parameter in the model, therefore no dose adjustment of IMFINZI is recommended for patients. The effect of severe renal impairment (CrCL 15 to 29 mL/min) on the PK of durvalumab is unknown (see ACTION AND CLINICAL PHARMACOLOGY).

Hepatic Impairment: A population PK analysis could not detect any effect of mild hepatic impairment on the CL parameter in the model, therefore no dose adjustment of IMFINZI is recommended for patients. IMFINZI has not been studied in patients with moderate or severe hepatic impairment (see ACTION AND CLINICAL PHARMACOLOGY).

3.2 Reconstitution and Administration

Preparation of Infusion Solution

IMFINZI is only to be administered by intravenous infusion.

IMFINZI is supplied as a single-use vial and does not contain any preservatives, therefore, aseptic technique must be observed.

Visually inspect drug product for particulate matter and discolouration. IMFINZI is a clear to opalescent, colourless to slightly yellow solution. Discard the vial if the solution is cloudy, discoloured or visible particles are observed. Do not shake the vial.

- Withdraw the required volume from the vial(s) of IMFINZI and transfer into an intravenous (IV) bag containing 0.9% Sodium Chloride Injection or 5% Dextrose Injection. Mix diluted solution by gentle inversion. The final concentration of the diluted solution should be between 1 mg / mL and 15 mg / mL.
- Do not freeze or shake the solution.
- No incompatibilities between IMFINZI and 0.9% Sodium Chloride or 5% Dextrose have been observed.
- IMFINZI must not be mixed with other drug products except those mentioned above.
- Care must be taken to ensure the sterility of prepared solutions.
- Do not re-enter the vial after withdrawal of drug. Only administer one dose per vial.
• Discard any unused portion left in the vial.

Storage of Infusion Solution

IMFINZI does not contain a preservative.

Administer infusion solution once prepared. If infusion solution is not administered immediately and it needs to be stored, the total time from vial puncture to the start of administration should not exceed:

• 24 hours under refrigeration at 2°C to 8°C, or
• 4 hours at room temperature at 15°C to 30°C

Administration of Infusion Solution

• Administer infusion solution intravenously over 60 minutes through an intravenous line containing a sterile, low-protein binding 0.2 or 0.22 micron in-line filter.

• Do not co-administer other drugs through the same infusion line. After each dose, flush the infusion line.

4 OVERDOSAGE

There is no specific treatment in the event of IMFINZI (durvalumab) overdose, and symptoms of overdose are not established. In the event of an overdose, healthcare practitioners should follow general supportive measures and should treat symptomatically.

For management of a suspected drug overdose, contact your regional poison control centre.

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 Dosage Forms, Strengths, Composition and Packaging

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Dosage Form / Strength/Composition</th>
<th>Non-medicinal Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous infusion</td>
<td>Single-use vial of:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 120 mg durvalumab / 2.4 mL</td>
<td>L-histidine, L-histidine</td>
</tr>
<tr>
<td></td>
<td>(nominal concentration of 50 mg/mL)</td>
<td>hydrochloride monohydrate,</td>
</tr>
<tr>
<td></td>
<td>• 500 mg durvalumab / 10 mL</td>
<td>Polysorbate 80, α,α-</td>
</tr>
<tr>
<td></td>
<td>(nominal concentration of 50 mg/mL)</td>
<td>trehalose dihydrate, and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Water for Injection.</td>
</tr>
</tbody>
</table>

Dosage Form Description

IMFINZI (durvalumab) injection is a sterile, preservative-free, clear to opalescent, colourless to slightly yellow solution, free from visible particles.
Packaging
10 mL of concentrate in a 10 mL Type I glass vial with an elastomeric stopper and a white flip-off aluminum seal contains 500 mg durvalumab. Pack size of 1 vial.

2.4 mL of concentrate in a 10 mL Type 1 glass vial with an elastomeric stopper and a gray flip-off aluminum seal contains 120 mg durvalumab. Pack size of 1 vial.

6 WARNINGS AND PRECAUTIONS

General
IMFINZI (durvalumab) should be administered under the supervision of healthcare practitioners experienced in the treatment of cancer.

Driving and Operating Machinery
Based on its pharmacodynamic properties, IMFINZI is unlikely to affect the ability to drive and use machines. However, if patients experience adverse reactions affecting their ability to concentrate and react, they should be advised not to drive or operate machinery.

Immune-Mediated Adverse Reactions
Adverse reactions observed with immunotherapies such as IMFINZI may differ from those observed with non-immunotherapies and may require immunosuppression. Early identification of adverse reactions and timely intervention are an important part of the safe use of IMFINZI. In clinical trials, most immune-mediated adverse reactions were reversible and managed with interruptions of IMFINZI, administration of corticosteroids and/or supportive care. Refer to DOSAGE AND ADMINISTRATION, Table 1 for recommended treatment modifications and management of immune-mediated adverse reactions.

Immune-Mediated Pneumonitis
Cases of immune-mediated pneumonitis or interstitial lung disease, including fatal cases, defined as requiring use of systemic corticosteroids and with no clear alternate etiology, occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Immune-Mediated Pneumonitis). Patients should be monitored for signs and symptoms of pneumonitis. Patients with suspected pneumonitis should be evaluated with radiographic imaging and managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

Immune-Mediated Hepatitis
Cases of immune-mediated hepatitis, including fatal cases, defined as requiring use of systemic corticosteroids and with no clear alternate etiology, occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Immune-Mediated Hepatitis). Patients should be monitored for abnormal liver function tests prior to each infusion with IMFINZI. Immune-mediated hepatitis should be managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

Immune-Mediated Colitis
Immune-mediated colitis or diarrhea, defined as requiring use of systemic corticosteroids and with no clear alternate etiology, occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Immune-Mediated Colitis). Patients should be monitored for signs and symptoms of colitis or diarrhea and managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.
Immune-Mediated Endocrinopathies

**Hypothyroidism:**
Immune-mediated hypothyroidism occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Immune-Mediated Endocrinopathies, Hypothyroidism). Patients should be monitored for abnormal thyroid function tests prior to each infusion or at least once per month during treatment. Manage hypothyroidism as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Hyperthyroidism:**
Immune-mediated hyperthyroidism (including thyroiditis) occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Immune-Mediated Endocrinopathies, Hyperthyroidism). Patients should be monitored for abnormal thyroid function tests prior to each infusion or at least once per month during treatment. Symptomatic hyperthyroidism should be managed as per institutional guidelines. See DOSAGE AND ADMINISTRATION, Table 1.

**Adrenal Insufficiency:**
Immune-mediated adrenal insufficiency occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Immune-Mediated Endocrinopathies, Adrenal Insufficiency). Patients should be monitored for clinical signs and symptoms of adrenal insufficiency. For symptomatic adrenal insufficiency, patients should be managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Hypophysitis:**
Immune-mediated hypophysitis has been observed in clinical trials of products that target PD-1/PD-L1, including IMFINZI. Patients should be monitored for signs and symptoms of hypophysitis. For symptomatic hypophysitis or hypopituitarism, patients should be managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Type I Diabetes Mellitus:**
Immune-mediated Type 1 diabetes mellitus (T1DM) has been observed in clinical trials of products that target PD-1/PD-L1, including IMFINZI. Monitor for signs and symptoms of T1DM. For symptomatic T1DM, patients should be managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Immune-Mediated Nephritis**
Immune-mediated nephritis, defined as requiring use of systemic corticosteroids and with no clear alternate etiology, occurred in patients receiving IMFINZI in clinical trials (see ADVERSE REACTIONS, Immune-Mediated Nephritis). Patients should be monitored for abnormal renal function tests prior to and periodically during treatment with IMFINZI and managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Immune-Mediated Rash**
Immune-mediated rash or dermatitis, defined as requiring use of systemic corticosteroids and with no clear alternate etiology, occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Immune-Mediated Rash). Patients should be monitored for signs and symptoms of rash or dermatitis and managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Other Immune-Mediated Adverse Reactions**
Given the mechanism of action of IMFINZI, other potential immune-mediated adverse reactions may occur. In clinical studies, rare cases (<0.1%) of potentially immune-related aseptic
meningitis, immune thrombocytopenic purpura (fatal), myocarditis, myositis, and uveitis were observed. Patients should be monitored for signs and symptoms of immune-mediated adverse reactions and managed as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Infection**
Severe infections, including sepsis, necrotizing fasciitis, and osteomyelitis, occurred in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS, Infections). Monitor patients for signs and symptoms of infection and treat with anti-infectives for suspected or confirmed infections as recommended in DOSAGE AND ADMINISTRATION, Table 1.

**Infusion Related Reactions**
Severe infusion related reactions have been reported in patients receiving IMFINZI in clinical studies (see ADVERSE REACTIONS). Patients should be monitored for signs and symptoms of infusion related reactions as recommended in DOSAGE AND ADMINISTRATION, Table 1. In patients with prior infusion related reactions to IMFINZI, pre-medication prior to administration may be considered.

**Sexual Health**

**Fertility**
There are no data on the potential effects of IMFINZI on fertility in humans. In repeat-dose toxicology studies with IMFINZI in sexually mature cynomolgus monkeys of up to 3 months duration, there were no notable effects on the male and female reproductive organs (see NON-CLINICAL TOXICOLOGY).

### 6.1 Special Populations

#### 6.1.1 Pregnant Women

There are no data on the use of IMFINZI in pregnant women. Based on its mechanism of action, IMFINZI has the potential to impact maintenance of pregnancy and may cause fetal harm when administered to a pregnant woman.

Human immunoglobulin G1 (IgG1) is known to cross the placental barrier. IMFINZI is not recommended during pregnancy. Women of childbearing potential should use effective contraception during treatment with IMFINZI and for at least 3 months after the last dose.

In animal reproduction studies, administration of IMFINZI to pregnant cynomolgus monkeys from the confirmation of pregnancy through delivery, at exposure levels approximately 6 to 20 times higher than those observed at the clinical dose of 10 mg/kg of IMFINZI (based on AUC) was associated with premature delivery, fetal loss (abortion and stillbirth) and an increase in neonatal deaths (see NON-CLINICAL TOXICOLOGY).

#### 6.1.2 Breast-feeding

There is no information regarding the presence of durvalumab in human milk, the absorption and effects on the breastfed infant, or the effects on milk production. Human IgG is excreted in human milk. In animal reproduction studies, administration of durvalumab to pregnant cynomolgus monkeys was associated with dose-related low level excretion of durvalumab in the breast milk of lactating cynomolgus monkeys, and was associated with premature neonatal death (see NON-CLINICAL TOXICOLOGY). Because of the potential for adverse reactions in
breastfed infants from durvalumab, breastfeeding is not recommended during treatment with IMFINZI and for at least 3 months after the last dose.

6.1.3 Pediatrics

Pediatrics (<18 years of age): The safety and efficacy of IMFINZI in patients younger than 18 years of age have not been established.

6.1.4 Geriatrics

Geriatrics (≥65 years of age): No dose adjustment is required for elderly patients (≥65 years of age). Of the 191 patients (primary efficacy population) treated with IMFINZI, 118 patients (61.8%) were 65 years of age or older. No overall clinically meaningful differences in safety or efficacy were reported between these patients (≥ 65 years) and younger patients (<65 years).

7 ADVERSE REACTIONS

7.1 Adverse Reaction Overview

Urothelial Carcinoma

The safety of IMFINZI (durvalumab) was evaluated in the urothelial carcinoma (UC) cohort of Study 1108. This cohort enrolled 191 patients in an open-label, single-arm trial with locally advanced or metastatic UC. Of the 191 patients enrolled, 182 patients had UC that had progressed during or after platinum-based chemotherapy or had progressed within 12 months of platinum-based neoadjuvant or adjuvant chemotherapy. Patients received 10 mg/kg IMFINZI via intravenous infusion every 2 weeks (Q2W) until disease progression or unacceptable toxicity. Treatment was continued for a maximum of 12 months. The median duration of exposure was 12 weeks (range: 1.6 to 54.3 weeks).

IMFINZI monotherapy 10 mg/kg Q2W was well tolerated in the UC population. Adverse reactions were generally manageable and reversible with interruption of dosing and treatment with immunosuppressants, such as corticosteroids.

Overall and regardless of relationship to treatment, an adverse event was experienced by 99.0% (189/191) of treated patients. At least one serious adverse event (SAE) was reported in 54.5% (104/191) of patients (for 12 of these patients, disease progression was reported as an SAE) and 9 (4.7%) patients had treatment-related SAE. The most common SAEs (occurring in ≥2% of patients) were back pain (4.7%), urinary tract infection (4.2%), acute kidney injury (4.2%), general physical health deterioration (3.7%), sepsis (3.1%), abdominal pain (2.6%), vomiting (2.6%), hypercalcemia (2.6%), and pyrexia (2.1%). Of the 191 enrolled UC patients, 15 (7.9%) had adverse events that resulted in death, including cardio-respiratory arrest, subileus, general physical deterioration, immune-mediated hepatitis, chronic hepatic failure, sepsis, cerebrovascular accident, acute kidney injury and pneumonitis. Of these, investigators considered one Grade 5 event each of pneumonitis and immune-mediated hepatitis to be related to treatment with durvalumab.

The most common adverse events regardless of relationship to treatment (any Grade; occurring in ≥10% of patients) were fatigue (35.6%), constipation (25.7%), decreased appetite (22.5%), nausea (22.0%), anemia (18.3%), diarrhea (16.8%), back pain (16.8%), urinary tract infection (16.2%), fever (15.7%), peripheral edema (14.1%), vomiting (13.1%), cough (11.5%), dyspnea (11.5%), increased blood creatinine (11.0%), arthralgia (10.5%) and asthenia (10.5%). The majority of adverse events were Grade 1 or 2 (mild to moderate) in severity; Grade 3 or 4 adverse events were reported in 52 (27.2%) patients. The most common Grade 3 or 4 adverse
events (>3% of patients) were anemia (9.9%), hyponatremia (5.8%), acute kidney injury (4.7%), urinary tract infection (4.2%), back pain (4.2%), fatigue, sepsis, hypercalcemia and asthenia (3.1% each). Treatment-related Grade 3 or 4 adverse events were reported in 6.8% of patients; the most common (≥1%) were increased AST (1.6%), increased ALT (1.0%), and increased GGT (1.0%), all of which were generally manageable and reversible.

Adverse events (excluding disease progression) leading to the delay, interruption or discontinuation of IMFINZI occurred in 68 (35.6%), 3 (1.6%), and 9 (4.7%) patients, respectively; the most common reasons for dose delay (occurring in >1% of patients) were back pain (3.7%), urinary tract infection (2.6%), acute kidney injury (1.6%), AST increased (1.6%), GGT increased (1.6%), and pneumonia (1.6%). The most common reason for dose discontinuation (occurring in ≥1% of patients) was general physical health deterioration in 2 (1.0%) patients.

7.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Table 3 lists the adverse drug reactions, with incidences regardless of investigators assessment of causality, reported in patients with UC (n=191) treated with IMFINZI 10 mg/kg Q2W.

Table 3 Adverse Drug Reactions in the Urothelial Carcinoma Patients Treated with IMFINZI at 10 mg/kg Q2W (Study 1108)

<table>
<thead>
<tr>
<th>System Organ Class Preferred Term</th>
<th>Any Grade N (%)</th>
<th>Grade 1 N (%)</th>
<th>Grade 2 N (%)</th>
<th>Grade 3 or 4 N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocarditis</td>
<td>Not reported&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism&lt;sup&gt;d&lt;/sup&gt;</td>
<td>13 (6.8%)</td>
<td>4 (2.1%)</td>
<td>9 (4.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Hyperthyroidism&lt;sup&gt;d&lt;/sup&gt;</td>
<td>9 (4.7%)</td>
<td>7 (3.7%)</td>
<td>2 (1.0%)</td>
<td>0</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>1 (0.5%)</td>
<td>1 (0.5%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypopituitarism</td>
<td>Not reported&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes insipidus</td>
<td>Not reported&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1 diabetes mellitus</td>
<td>Not reported&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### System Organ Class
#### Preferred Term

<table>
<thead>
<tr>
<th>IMFINZI (N=191)</th>
<th>Any Grade</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3 or 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>32 (16.8%)</td>
<td>22 (11.5%)</td>
<td>9 (4.7%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Colitis&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2 (1.0%)</td>
<td>1 (0.5%)</td>
<td>1 (0.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis&lt;sup&gt;b,d&lt;/sup&gt;</td>
<td>3 (1.6%)</td>
<td>1 (0.5%)</td>
<td>0</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased&lt;sup&gt;d&lt;/sup&gt;</td>
<td>16 (8.4%)</td>
<td>8 (4.2%)</td>
<td>3 (1.6%)</td>
<td>5 (2.6%)</td>
</tr>
<tr>
<td>Alanine aminotransferase increased&lt;sup&gt;d&lt;/sup&gt;</td>
<td>16 (8.4%)</td>
<td>10 (5.2%)</td>
<td>3 (1.6%)</td>
<td>3 (1.6%)</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion related reaction</td>
<td>2 (1.0%)</td>
<td>1 (0.5%)</td>
<td>0</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood creatinine increased</td>
<td>21 (11.0%)</td>
<td>14 (7.3%)</td>
<td>6 (3.1%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Nephritis&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1 (0.5%)</td>
<td>0</td>
<td>0</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonitis&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2 (1.0%)</td>
<td>1 (0.5%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>Not reported&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash&lt;sup&gt;d&lt;/sup&gt;</td>
<td>27 (14.1%)</td>
<td>20 (10.5%)</td>
<td>6 (3.1%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Pruritus&lt;sup&gt;d&lt;/sup&gt;</td>
<td>12 (6.3%)</td>
<td>9 (4.7%)</td>
<td>3 (1.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>1 (0.5%)</td>
<td>0</td>
<td>1 (0.5%)</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup> Incidences presented in this table are based on reports of drug-related adverse events.

<sup>b</sup> Including a fatal outcome.

<sup>c</sup> Adverse Drug Reactions not reported in the UC cohort but reported from other clinical studies (N=1779) included interstitial lung disease: uncommon (≥1/1,000 to <1/100) in any grade, and uncommon in Grade 3 or 4. Type 1 diabetes mellitus, hypopituitarism including diabetes insipidus, myocarditis: rare (≥1/10,000 to <1/1000) in any grade, rare in Grade 3 or 4.

<sup>d</sup> Included additional preferred terms: aspartate aminotransferase increased or alanine aminotransferase increased included transaminase increased and hepatic enzyme increased; colitis included enterocolitis, proctitis and enteritis; hepatitis included autoimmune hepatitis, hepatitis toxic, hepatocellular injury, hepatitis acute and hepatotoxicity; hypothyroidism included autoimmune hypothyroidism; hyperthyroidism included autoimmune thyroiditis, thyroiditis, thyroiditis subacute, Basedow's disease; rash included rash erythematous, rash generalized, rash macular, rash maculopapular, rash papular, rash pruritic, rash pustular, erythema, and eczema; pruritus included pruritus generalized; nephritis included autoimmune nephritis, glomerulonephritis, tubulointerstitial nephritis.

Table 4 lists the incidences of very common (occurring in ≥10% of patients) adverse events, regardless of investigators assessment of causality, reported in patients with UC (n=191)
treated with IMFINZI 10 mg/kg Q2W.

Table 4  Adverse Events Reported in ≥10% in Urothelial Carcinoma Patients Treated with IMFINZI at 10 mg/kg Q2W (Study 1108)

<table>
<thead>
<tr>
<th>System Organ Class Preferred Term*</th>
<th>IMFINZI (N =191)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade N (%)</td>
</tr>
<tr>
<td><strong>Blood and lymphatic system disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>35 (18.3%)</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>49 (25.7%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>41 (21.5%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>25 (13.1%)</td>
</tr>
<tr>
<td><strong>General disorders and administration site conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>68 (35.6%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>30 (15.7%)</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>27 (14.1%)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>20 (10.5%)</td>
</tr>
<tr>
<td><strong>Infections and infestations</strong></td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>31 (16.3%)</td>
</tr>
<tr>
<td><strong>Metabolism and nutrition disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>43 (22.5%)</td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>32 (16.8%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>20 (10.5%)</td>
</tr>
<tr>
<td><strong>Respiratory, thoracic and mediastinal disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>22 (11.6%)</td>
</tr>
<tr>
<td>Cough</td>
<td>21 (11.5%)</td>
</tr>
</tbody>
</table>

* The terms presented in the table are adverse events reported regardless of the investigators assessment of relationship to treatment.

Additional Information on Selected Adverse Reactions
The data for the following immune-mediated adverse reactions, defined as requiring the use of systemic corticosteroids/hormone replacement therapy with no clear alternate etiology, reflect exposure to IMFINZI, as a single agent, in Study 1108 (UC cohort (n=191) and overall population (n=970)) (see CLINICAL TRIALS). The management guidelines for these adverse reactions are described in WARNINGS AND PRECAUTIONS and DOSAGE AND
ADMINISTRATION.

Immune-Mediated Pneumonitis
In the UC cohort (n=191) of Study 1108, immune-mediated pneumonitis occurred in 1 (0.5%) patient (Grade 5).

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated pneumonitis occurred in 8 (0.8%) patients, including Grade 3 in 1 patient (0.1%), Grade 4 in 1 (0.1%) patient, and Grade 5 in 1 (0.1%) patient. The median time to onset was 76 days (range: 24-237 days). All 8 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). IMFINZI was discontinued in 2 patients. Resolution occurred in 3 patients.

Immune-Mediated Hepatitis
In the UC cohort (n=191) of Study 1108, immune-mediated hepatitis occurred in 4 (2.1%) patients, with Grade 3 in 2 (1.0%) patients, and Grade 5 in 1 (0.5%) patient.

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated hepatitis occurred in 14 (1.4%) patients, including Grade 3 in 7 (0.7%) patients and Grade 5 in 1 (0.1%) patient. The median time to onset was 81.5 days (range: 15-312 days). Ten of the 14 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). One patient also received mycophenolate treatment. IMFINZI was discontinued in 3 patients. Resolution occurred in 6 patients.

Immune-Mediated Colitis
In the UC cohort (n=191) of Study 1108, immune-mediated colitis or diarrhea occurred in 4 (2.1%) patients (diarrhea in 4 patients [2.1%, Grade 1 or 2]) and colitis occurred in 1 patient (0.5%, Grade 2).

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated colitis or diarrhea occurred in 19 (2.0%) patients, including Grade 3 in 3 patients (0.3%) and Grade 4 in 1 (0.1%) patient. The median time to onset was 93.0 days (range: 1-345 days). Ten of the 19 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). One patient also received infliximab treatment. IMFINZI was discontinued in 5 patients. Resolution occurred in 12 patients.

Immune-Mediated Endocrinopathies
Hypothyroidism
In the UC cohort (n=191) of Study 1108, immune-mediated hypothyroidism occurred in 10 (5.2%) patients, there were no Grade 3 or 4 cases.

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated hypothyroidism occurred in 58 (6.0%) patients, there were no Grade 3 or 4 cases. The median time to onset was 71 days (range: 9-269 days). Of the 58 patients, 55 patients received hormone replacement therapy, 1 patient received high-dose corticosteroids (at least 40 mg prednisone or equivalent per day) for hypothyroidism followed by hormone replacement. No patient discontinued IMFINZI due to hypothyroidism.
Hyperthyroidism
In the UC cohort (n=191) of Study 1108, immune-mediated hyperthyroidism occurred in 2 (1.0%) patients (Grade 2).

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated hyperthyroidism occurred in 9 (0.9%) patients, there were no Grade 3 or 4 cases. The median time to onset was 43 days (range: 27-106 days). Of these 9 patients, 4 patients received medical therapy (thiamazole), 1 patient received thyroxine when hyperthyroidism transitioned to hypothyroidism, 4 patients received systemic corticosteroids and 1 of the 4 patients received high-dose systemic corticosteroid treatment (at least 40 mg prednisone or equivalent per day). No patients discontinued IMFINZI due to hyperthyroidism. Resolution occurred in 6 patients. Some patients may have hypothyroidism following hyperthyroidism.

Adrenal Insufficiency
In the UC cohort (n=191) of Study 1108, immune-mediated adrenal insufficiency occurred in 1 (0.5%) patient (Grade 1).

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated adrenal insufficiency occurred in 5 (0.5%) patients, there were no Grade 3 or 4 cases. The median time to onset was 136 days (range: 70-265 days). All 5 patients received systemic corticosteroids; 1 of the 5 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). No patients discontinued IMFINZI due to adrenal insufficiency.

Hypophysitis
In clinical studies, hypopituitarism (including diabetes insipidus) was observed in one patient (less than 0.1%) treated with IMFINZI. This patient received high dose corticosteroid and did not discontinue IMFINZI.

Type I Diabetes Mellitus
In clinical studies, Type I diabetes mellitus was observed in one patient (less than 0.1%) treated with IMFINZI. This patient received insulin treatment and discontinued IMFINZI.

Immune-Mediated Nephritis
In the UC cohort (n=191) of Study 1108, immune-mediated nephritis occurred in 1 (0.5%) patient (Grade 3).

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated nephritis occurred in 4 (0.4%) patients, including Grade 3 in 2 (0.2%) patients. The median time to onset was 89 days (range: 71 to 239 days). Three of the 4 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). IMFINZI was discontinued in 3 patients. Resolution occurred in 3 patients.

Immune-Mediated Rash
In the UC cohort (n=191) of Study 1108, immune-mediated rash or dermatitis occurred in 2 (1%) patients, including Grade 3 in 1 (0.5%) patient.

In the overall population of Study 1108 (n=970, multiple tumour types including UC cohort) with IMFINZI monotherapy, immune-mediated rash or dermatitis occurred in 13 (1.3%) patients,
including Grade 3 in 3 (0.3%) patients. The median time to onset was 43 days (range: 4 to 280 days). Four of the 13 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). No patients discontinued IMFINZI due to immune-mediated rash or dermatitis. Resolution occurred in 5 patients.

7.3 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Changes in laboratory parameters were predominantly Grade 1 or 2 in severity, and the incidence of any grade worsening to Grade 3 or 4 was generally low (Table 5).

Table 5  Laboratory Abnormalities Worsened from Baseline Occurring in ≥1% (Grade 3 or 4) of IMFINZI-Treated Patients with Urothelial Carcinoma (Study 1108)

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>IMFINZI (N=191)</th>
<th>Grades 1 N (%)</th>
<th>Grades 2 N (%)</th>
<th>Grade 3 or 4a N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>180</td>
<td>25 (13.9%)</td>
<td>38 (21.1%)</td>
<td>22 (12.2%)</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>179</td>
<td>62 (34.6%)</td>
<td>0</td>
<td>19 (10.6%)</td>
</tr>
<tr>
<td>Lymphocyte count decreased</td>
<td>180</td>
<td>20 (11.1%)</td>
<td>41 (22.8%)</td>
<td>19 (10.6%)</td>
</tr>
<tr>
<td>Hypermagnesemia</td>
<td>176</td>
<td>13 (7.4%)</td>
<td>0</td>
<td>7 (4.0%)</td>
</tr>
<tr>
<td>Alkaline phosphatase increased</td>
<td>179</td>
<td>28 (15.6%)</td>
<td>15 (8.4%)</td>
<td>7 (3.9%)</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>179</td>
<td>35 (19.6%)</td>
<td>5 (2.8%)</td>
<td>7 (3.9%)</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>176</td>
<td>16 (9.1%)</td>
<td>4 (2.3%)</td>
<td>6 (3.4%)</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>178</td>
<td>47 (26.4%)</td>
<td>26 (14.6%)</td>
<td>6 (3.4%)</td>
</tr>
<tr>
<td>Blood bilirubin increased</td>
<td>179</td>
<td>9 (5.0%)</td>
<td>6 (3.4%)</td>
<td>4 (2.2%)</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>179</td>
<td>21 (11.7%)</td>
<td>8 (4.5%)</td>
<td>4 (2.2%)</td>
</tr>
<tr>
<td>Creatinine increased</td>
<td>180</td>
<td>40 (22.2%)</td>
<td>16 (8.9%)</td>
<td>4 (2.2%)</td>
</tr>
<tr>
<td>Alanine aminotransferase increased</td>
<td>180</td>
<td>27 (15.0%)</td>
<td>6 (3.3%)</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>178</td>
<td>5 (2.8%)</td>
<td>7 (3.9%)</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>179</td>
<td>34 (19.0%)</td>
<td>31 (17.3%)</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>179</td>
<td>16 (8.9%)</td>
<td>0</td>
<td>2 (1.1%)</td>
</tr>
</tbody>
</table>

a  Frequency of lab abnormalities for Grade 1 and Grade 2 are provided for those lab abnormalities reported in ≥1% patients with Grade 3 and Grade 4 severity.

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity.

Due to assay deficiencies, the immunogenicity of IMFINZI has not yet been adequately established. Of 1169 patients who were treated with IMFINZI 10 mg/kg every 2 weeks across trials and evaluable for the presence of anti-drug antibodies (ADAs), 3.3% (38/1169) patients tested positive for treatment-emergent ADAs. Neutralizing antibodies against durvalumab were detected in 0.2% (2/1169) patients. A population PK analysis could not detect any clinically relevant effect of ADAs on the PK parameters in the model.
Immunogenicity assay results are highly dependent on several factors, including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications and underlying disease. For these reasons, comparison of incidence of antibodies to IMFINZI with the incidence of antibodies to other products may be misleading.

8 DRUG INTERACTIONS

The drug interaction potential of IMFINZI (durvalumab) is unknown. No formal pharmacokinetic drug-drug interaction studies have been conducted with durvalumab as durvalumab is an immunoglobulin.

9 ACTION AND CLINICAL PHARMACOLOGY

9.1 Mechanism of Action

Expression of programmed cell death ligand-1 (PD-L1) protein is an adaptive immune response that helps tumours evade detection and elimination by the immune system. PD-L1 expression can be induced by inflammatory signals (e.g., IFN-gamma) and can be expressed on both tumour cells and tumour-associated immune cells present in the tumour microenvironment. Through its interactions with PD-1 and CD80 (B7.1), PD-L1 reduces cytotoxic T-cell activity, proliferation, and cytokine production.

IMFINZI (durvalumab) is a fully human, high affinity, immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that selectively blocks the interaction of PD-L1 with PD-1 and CD80 (B7.1) while leaving PD-1/PD-L2 interaction intact. IMFINZI does not induce antibody dependent cell-mediated cytotoxicity (ADCC). Selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses.

In preclinical studies, PD-L1 blockade led to increased T-cell activation and delayed tumour growth.

9.2 Pharmacokinetics

The pharmacokinetics (PK) of IMFINZI was studied in 1324 patients with solid tumours with doses ranging from 0.1 to 20 mg/kg administered once every two, three or four weeks. PK exposure increased more than dose-proportionally (non-linear PK) at doses <3 mg/kg and dose proportionally (linear PK) at doses ≥ 3 mg/kg. Steady state was achieved at approximately 16 weeks.

Based on population PK analysis that included 1310 patients (dose ≥ 10 mg/kg), the mean steady-state clearance, steady state volume of distribution, and terminal half-life were 8.24 mL/h, 5.6 L, and approximately 17 days, respectively. Following multiple doses, the systemic accumulation in area under the curve (AUC), maximum concentration (C_{max}) and trough concentration (C_{min}) was 2.6, 1.9, and 3.2-fold, respectively.

Durvalumab clearance decreases over time, with a mean maximal reduction (% coefficient of variation [CV%]) from baseline values of approximately 22.9% (46.3%). The decrease in CLss was not considered clinically relevant.
Special Populations and Conditions

The covariate of age (19–96 years), body weight (34-149 Kg), gender, positive anti-drug antibody (ADA) status, albumin levels, LDH levels, creatinine levels, soluble PD-L1, tumour type, race, mild renal impairment (creatinine clearance (CrCL) 60 to 89 mL/min), moderate renal impairment (creatinine clearance (CrCL) 30 to 59 mL/min), mild hepatic impairment (bilirubin ≤ ULN and AST > ULN or bilirubin >1.0 to 1.5 × ULN and any AST), or ECOG status were shown to have no clinically significant effect on the pharmacokinetics parameters in the population PK model of durvalumab.

Hepatic Insufficiency: The effect of moderate hepatic impairment (bilirubin >1.5 to 3 x ULN and any AST) or severe hepatic impairment (bilirubin >3.0 x ULN and any AST) on the pharmacokinetics of durvalumab is unknown.

Renal Insufficiency: The effect of severe renal impairment (CrCL 15 to 29 mL/min) on the pharmacokinetics of durvalumab is unknown.

10 STORAGE, STABILITY AND DISPOSAL

Store IMFINZI (durvalumab) under refrigeration at 2°C to 8°C. Protect IMFINZI from light by storing in the original package until time of use. Do not freeze or shake. For storage conditions after preparation of the infusion, see DOSAGE AND ADMINISTRATION, Storage of Infusion Solution.

11 SPECIAL HANDLING INSTRUCTIONS

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
12 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Durvalumab

Structure: Durvalumab is a fully human monoclonal antibody of the immunoglobulin (Ig) G1 kappa subclass composed of 2 identical heavy chains and 2 identical light chains.

Molecular formula and molecular mass: Approximately 149 kDa, including oligosaccharides.

Physicochemical properties: The durvalumab drug substance is a clear to opalescent, colourless to slightly yellow liquid with a density of 1.054 mg/mL. The durvalumab drug substance liquid is formulated in buffer (26 mM histidine/histidine-HCl, 275 mM trehalose dihydrate, 0.02% (w/v) polysorbate 80, pH 6.0) at a concentration of 50 mg/mL (nominal). The pI of durvalumab is 8.1-8.8.

13 CLINICAL TRIALS

Urothelial Carcinoma

The efficacy of IMFINZI (durvalumab), in terms of tumour response rate, was evaluated in a Phase I/II, global, multicenter, multi-cohort, open-label, single-arm clinical trial, Study 1108. In the urothelial carcinoma (UC) cohort, 191 patients received IMFINZI 10 mg/kg every 2 weeks (Q2W). Patients were followed for at least 16 weeks as of the data cut-off date (had tumour assessments at Weeks 6, 12 and 16). The reported efficacy is based on 182 patients with locally advanced or metastatic UC who had progression during or after platinum-containing chemotherapy, including those patients who progressed within 12 months of receiving therapy in a neo-adjuvant or adjuvant setting. The remaining 9 patients were treatment naïve/first line. The median duration of follow-up for the 182 patients who had received prior platinum-based chemotherapy was 5.57 months (range: 0.4 to 25.9 months).

IMFINZI 10 mg/kg was administered by intravenous infusion every 2 weeks for up to 12 months.
or until unacceptable toxicity or confirmed disease progression. In the absence of clinical deterioration, patients in the UC cohort were permitted to continue to receive IMFINZI after confirmed progression of disease if investigators considered that they continued to derive a clinical benefit. The primary efficacy endpoint was Objective Response Rate (ORR) according to RECIST v1.1 as assessed by Blinded Independent Central Review (BICR). The trial excluded patients with a history of immunodeficiency; medical conditions that required systemic immunosuppression; history of severe immune-mediated adverse reactions; untreated CNS metastases; HIV; active tuberculosis, or hepatitis B or C infection. Additional efficacy endpoints included Duration of Response (DoR), Disease-Control Rate (DCR) and Overall Survival (OS).

In Study 1108, tumour specimens were evaluated for PD-L1 expression using the VENTANA PD-L1 (SP263 clone) immunohistochemical assay. Testing was performed prospectively at a central laboratory by pathologists trained in the use of the SP263 assay for the evaluation of PD-L1 expression. The test detects membrane and cytoplasmic PD-L1 expression by tumour cells (TC) and tumour-associated immune cells (IC). PD-L1 status was determined by the percentage of TC with any membrane PD-L1 staining above background or by the percentage of IC with PD-L1 staining (IC+) at any intensity above background. The percent of tumour area occupied by any tumour-associated immune cells (Immune Cells Present, ICP) is used to determine IC+, which is the percent area of ICP exhibiting PD-L1 positive immune cell staining. PD-L1 status is considered high if any of the following are met:

- ≥25% of tumour cells exhibit membrane staining; or,
- ICP >1% and IC+ ≥25%; or,
- ICP ≤ 1% and IC+ = 100%

If none of these criteria were met, PD-L1 status was considered low/negative.

Of the 182 patients that had received prior platinum-based chemotherapy, 95 were classified as PD-L1 high, 73 as PD-L1 low/negative and 14 patients were not evaluable for PD-L1 status.

### 13.1 Trial Design and Study Demographics

**Table 6**  Summary of Patient Demographics in the UC cohort of Study 1108 (N=182)

<table>
<thead>
<tr>
<th>Study #</th>
<th>Trial design</th>
<th>Dosage, route of administration and duration</th>
<th>Study subjects (n)</th>
<th>Mean age (Range)</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD-ON-MEDI4736-1108</td>
<td>Phase 1/2, multicenter, open-label, first-time-in-human, dose-escalation, dose-exploration, and dose-expansion study</td>
<td>10 mg/kg Q2W, intravenous, 12 months</td>
<td>182</td>
<td>66.2 years old</td>
<td>F: 51 (28.0%) M: 131 (72.0%)</td>
</tr>
</tbody>
</table>

In the UC cohort (n = 182), 70% of patients received prior cisplatin, 30% had prior carboplatin and 35% received 2 or more prior lines of systemic therapy. Seventy-four patients (42%) had a baseline creatinine clearance of <60 mL/min. The median age of patients was 67 years (range: 34 to 88), 72% were male, 71% were Caucasian, 22% were Asian, 4% were Black/African American and 3% were Other. Based on combined independent radiographic assessment and
investigator reported data, ninety-two percent (92%) had visceral metastases at study entry, including 43% with liver metastases. Lymph-node-only metastases were present in 8% of patients. Most patients had an ECOG performance status of 1 (66.5%), the remaining had ECOG status of 0 (33.5%). The Bellmunt risk score (which includes ECOG score, baseline hemoglobin, and liver metastases) was 0 in 22%, 1 in 38%, 2 in 30%, and 3 in 11% of patients.

13.2 Study Results

Table 7 summarizes the efficacy results for pre-specified analyses.

Overall, the ORR in the UC cohort was 17.6%. Patients with PD-L1 high tumours were associated with numerically increased ORR (27.4%).

Responses occurred early in the treatment. Median time to response was 1.40 months (range: 1.2 to 3.2 months), which coincides with the first protocol-specified imaging assessment. Responses appear durable; median DoR has not yet been reached (range: 0.9+ to 19.9+ months). Among the total 32 responding patients, 75.0% (24/32) had ongoing responses at the time of analysis for ORR (patients with ≥ 13 weeks follow-up), 15 (46.9%) patients had ongoing responses of 6 months or longer in duration, 10 (31.3%) patients had ongoing responses of 9 months or longer in duration and 5 (15.6%) patients had ongoing response of 12 months or longer in duration. Eight patients in the UC cohort did not have ongoing responses at the time of analysis. Seven patients progressed per BICR after an initial response. Of the 7 patients who progressed per BICR after an initial response, 3 patients continued on IMFINZI, and 4 patients completed 12 months of treatment with IMFINZI.

Table 7 Efficacy Results of Study 1108 in the UC Cohort (N=182) and by PD-L1 Status

<table>
<thead>
<tr>
<th>Efficacy Parametera</th>
<th>All Patients (N=182)</th>
<th>PD-L1 High (N=95)</th>
<th>PD-L1 Low/Negative (N=73)</th>
<th>PD-L1 NE (N=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of confirmed responders by BICR</td>
<td>32</td>
<td>26</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Objective Response Rate (95% CI)</td>
<td>17.6% (12.3%, 23.9%)</td>
<td>27.4% (18.7%, 37.5%)</td>
<td>4.1% (0.9%, 11.5%)</td>
<td>21.4% (4.7%, 50.8%)</td>
</tr>
<tr>
<td>CR, n (%)</td>
<td>6 (3.3%)</td>
<td>4 (4.2%)</td>
<td>1 (1.4%)</td>
<td>1 (7.1%)</td>
</tr>
<tr>
<td>PR, n (%)</td>
<td>26 (14.3%)</td>
<td>22 (23.2%)</td>
<td>2 (2.7%)</td>
<td>2 (14.3%)</td>
</tr>
<tr>
<td>Median DoR, months, range</td>
<td>NR (0.9+, 19.9+)</td>
<td>NR (0.9+, 19.9+)</td>
<td>12.25 (1.9+, 12.3)</td>
<td>NR (2.3+, 2.6+)</td>
</tr>
</tbody>
</table>

CR = Complete Response; PR = Partial Response; BICR = Blinded Independent Central Review; DoR = Duration of Response; TC = Tumour Cell; IC = Immune Cell; NE = Not Estimable; NR = Not Reached

14 NON-CLINICAL TOXICOLOGY

Carcinogenicity and Mutagenicity: The carcinogenic and genotoxic potential of durvalumab have not been evaluated.

Reproductive Toxicology: As reported in the literature, the PD-1/PD-L1 pathway plays a
central role in preserving pregnancy by maintaining maternal immune tolerance to the fetus, and in mouse allogeneic pregnancy models disruption of PD-L1 signaling was shown to result in an increase in fetal loss. In reproduction studies in cynomolgus monkeys, administration of IMFINZI (durvalumab) from the confirmation of pregnancy through delivery at exposure levels approximately 6 to 20 times higher than those observed at the clinical dose of 10 mg/kg of IMFINZI (based on AUC) was associated with premature delivery, fetal loss (abortion and stillbirth) and an increase in neonatal deaths. Based on the mechanism of action, fetal exposure to durvalumab may increase the risk of developing immune-mediated disorders or altering the normal immune response, and immune-mediated disorders have been reported in the literature in PD-1 knockout mice. In animal models reported in the literature, inhibition of PD-L1/PD-1 signaling increased the severity of some infections and enhanced inflammatory responses.
IMFINZI® (im-FIN-zee)  
durvalumab for injection, intravenous infusion

Read this information carefully before you start treatment with IMFINZI and each time you get an infusion. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about IMFINZI.

What is IMFINZI used for?
IMFINZI (durvalumab) is a medicine used to treat adults with a bladder cancer (called urothelial carcinoma) including cancer of the ureter, urethra or kidney pelvis. It contains the active substance durvalumab which belongs to the monoclonal antibody class of anticancer medicines. It is used when:
  • Your cancer has spread and cannot be removed by surgery and,
  • You have received chemotherapy, and it did not work or is no longer working.

For the following indication(s) IMFINZI has been approved with conditions (NOC/c). This means it has passed Health Canada’s review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

IMFINZI (durvalumab) is used to treat adults with a bladder cancer (called urothelial carcinoma) including cancer of the ureter, urethra or kidney pelvis. It is used when:
  • Your cancer has spread and cannot be removed by surgery and,
  • You have received chemotherapy, and it did not work or is no longer working.

What is a Notice of Compliance with Conditions (NOC/c)?
A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug’s performance after it has been sold, and to report their findings to Health Canada.
How does IMFINZI work?
- IMFINZI works by helping your immune system fight your cancer.
- IMFINZI can help slow or stop your cancer from growing. It can also help shrink the tumour. The average time to respond to IMFINZI is approximately 1.5 months. However, this may vary from patient to patient.

If you have any questions about how IMFINZI works or why this medicine has been prescribed for you, ask your healthcare professional.

What are the ingredients in IMFINZI?
Medicinal ingredient: durvalumab.
Non-medicinal ingredients: L-histidine, L-histidine hydrochloride monohydrate, α,α-trehalose dihydrate, polysorbate 80, and water for injection.

IMFINZI comes in the following dosage forms:
Glass single-use vials containing 120 mg (in 2.4 mL) or 500 mg (in 10 mL) of durvalumab.

Do not use IMFINZI if:
- You are allergic to durvalumab or any other ingredients in IMFINZI.

To help avoid unnecessary side effects and ensure proper use, talk to your healthcare professional before you take IMFINZI. Talk about any health conditions or problems you may have, including if you:
- Have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- Have had an organ transplant
- Have lung or breathing problems
- Have liver problems
- Have problems with hormone producing glands such as your thyroid, pituitary, adrenal glands or pancreas
- Have diabetes
- Are taking medicine(s) that affect the immune system such as a steroid

If you have any questions about your medical condition, talk to your healthcare professional.

When you receive IMFINZI, you can have some serious side effects.
IMFINZI can cause your immune system to attack normal organs and tissues in your body and can affect the way they work.

Other warnings you should know about:
Pregnancy
- If you are pregnant, think you may be pregnant or are planning to have a baby, tell your doctor before taking this medicine. You should not use IMFINZI if you are pregnant.
- IMFINZI can harm your unborn baby.
- If you are a woman who could become pregnant, you should use an effective method of birth control during your treatment and for at least 3 months after the last dose of IMFINZI.

Breastfeeding
- If you are breastfeeding or plan to breastfeed, tell your doctor.
- Do not breastfeed during treatment and for at least 3 months after the last dose of IMFINZI.
is not known if IMFINZI passes into your breast milk.

Driving and using machines
IMFINZI is unlikely to affect the ability to drive and use machines. However, if you experience side effects affecting your ability to concentrate and react, do not drive or use machines until you feel better.

Tell your healthcare professional about all the medicines you take, have recently taken or might take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take IMFINZI:
- IMFINZI will be given to you in a hospital or clinic under the supervision of an experienced doctor. Your doctor will give you IMFINZI through an IV (intravenous infusion into your vein) for about 60 minutes.
- IMFINZI is typically given every 2 weeks.
- Your doctor will decide how many treatments you need.

If you have any questions about your treatment, ask your doctor.

Usual dose:
The recommended dose is 10 mg of durvalumab per kilogram of your body weight.

It is not known if IMFINZI is safe and effective in children less than 18 years of age.

Overdose:
If you think you have taken too much IMFINZI, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
It is very important that you keep all your appointments to get IMFINZI. If you miss an appointment, call your doctor as soon as possible to discuss next steps.

What are possible side effects from using IMFINZI?
Like all medicines, this medicine can cause side effects, although not everybody gets them. These are not all the possible side effects you may feel when taking IMFINZI. If you get any side effects, talk to your doctor, pharmacist or nurse. If you experience any side effects not listed here, contact your healthcare professional.

Most frequent serious side effects:
- urinary tract infection
- acute kidney injury
- back pain
- general physical health deterioration

Most common side effects:
- feeling tired
- decreased appetite
• diarrhea
• joint pain
• fever
• nausea
• rash or itchiness

If you have any of the following, call or see your healthcare professional right away. Your healthcare professional may give you other medicines in order to prevent more severe complications and reduce your symptoms. Your healthcare professional may withhold the next dose of IMFINZI or stop your treatment with IMFINZI.

<table>
<thead>
<tr>
<th>Symptom / effect</th>
<th>Talk to your healthcare professional</th>
<th>Only if severe</th>
<th>In all cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lung problems (pneumonitis).</strong> Signs and symptoms of pneumonitis may include:</td>
<td></td>
<td></td>
<td>✓</td>
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<tr>
<td>• new or worsening cough</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• shortness of breath</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• chest pain</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Liver problems (hepatitis).</strong> Signs and symptoms of hepatitis may include:</td>
<td></td>
<td></td>
<td>✓</td>
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<tr>
<td>• yellowing of your skin or the whites of your eyes</td>
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<tr>
<td>• severe nausea or vomiting</td>
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<tr>
<td>• pain on the right side of your stomach area (abdomen)</td>
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<tr>
<td>• drowsiness</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• dark urine (tea coloured)</td>
<td></td>
<td></td>
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<tr>
<td>• bleeding or bruising more easily than normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• feeling less hungry than usual</td>
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<tr>
<td><strong>Intestinal problems (colitis) that can lead to tears or holes in your intestine.</strong> Signs and symptoms of colitis may include:</td>
<td></td>
<td></td>
<td>✓</td>
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<tr>
<td>• diarrhea or more bowel movements than usual</td>
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<tr>
<td>• stools that are black, tarry, sticky, or have blood or mucus</td>
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<tr>
<td>• severe stomach area (abdomen) pain or tenderness</td>
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<tr>
<td><strong>Hormone gland problems (especially the thyroid, adrenals, pituitary and pancreas).</strong> Signs and symptoms that your hormone glands especially the thyroid gland is not working properly may include:</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>• headaches that will not go away or unusual headaches</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Serious side effects and what to do about them

<table>
<thead>
<tr>
<th>Symptom / effect</th>
<th>Talk to your healthcare professional</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Only if severe</td>
</tr>
<tr>
<td></td>
<td>In all cases</td>
</tr>
<tr>
<td>• extreme tiredness</td>
<td></td>
</tr>
<tr>
<td>• weight gain or weight loss</td>
<td></td>
</tr>
<tr>
<td>• dizziness or fainting</td>
<td></td>
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<tr>
<td>• feeling more hungry or thirsty than usual</td>
<td></td>
</tr>
<tr>
<td>• hair loss</td>
<td></td>
</tr>
<tr>
<td>• feeling cold</td>
<td></td>
</tr>
<tr>
<td>• constipation</td>
<td></td>
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<tr>
<td>• your voice gets deeper</td>
<td></td>
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<tr>
<td>• urinating more often than usual</td>
<td></td>
</tr>
<tr>
<td>• nausea or vomiting</td>
<td></td>
</tr>
<tr>
<td>• stomach area (abdomen) pain</td>
<td></td>
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<tr>
<td>• changes in mood or behaviour, such as decreased sex drive, irritability, or</td>
<td></td>
</tr>
<tr>
<td>forgetfulness</td>
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</tr>
</tbody>
</table>

**Kidney problems, including nephritis and kidney failure.**

Signs of kidney problems may include:

- decrease in the amount of urine
- blood in your urine
- swelling in your ankles
- loss of appetite

**Skin problems.**

Signs of these problems may include:

- rash
- itching
- skin blistering
- ulcers in mouth or other mucous membranes

**Problems in other organs.**

Signs of these problems may include:

- changes in eyesight
- severe or persistent muscle or joint pains
- severe muscle weakness
- chest pain, shortness of breath, irregular heartbeat (myocarditis)

**Severe infusion reactions.**

Signs and symptoms of severe infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing dizziness
- fever
- feeling like passing out
- back or neck pain
- facial swelling
If you have a side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

**Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp- mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

**NOTE:** Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

**Storage:**

IMFINZI should not be used after the expiry date which is stated on the label and carton. IMFINZI should be stored in a refrigerator (2° to 8°C) in the original package in order to protect from light. Do not freeze or shake. Any unused medicine or waste material should be disposed of in accordance with local requirements.

Keep medication out of reach and sight of children.

**If you want more information about IMFINZI:**

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); the manufacturer’s website www.astrazeneca.ca, or by calling 1-800-668-6000.
- This Patient Medication Information is current at the time of printing. The most up-to-date version can be found at www.astrazeneca.ca.

This leaflet was prepared by AstraZeneca Canada Inc., Mississauga, Ontario L4Y 1M4.

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