**DRUG NAME:** Durvalumab

**SYNONYM(S):** MEDI4736

**COMMON TRADE NAME(S):** IMFINZI®

**CLASSIFICATION:** monoclonal antibody

*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.*

**MECHANISM OF ACTION:**
Durvalumab is a fully human immunoglobulin G1 kappa monoclonal antibody that blocks the interaction between programmed death ligand 1 (PD-L1) and programmed death 1 (PD-1) and CD80. PD-L1 blockade enhances antitumour immune responses and leads to increased T-cell activation and delayed tumour growth.

**USES:**

*Primary uses:*
- Urothelial carcinoma
- Lung cancer, non-small cell
- Health Canada approved indication

*Other uses:*

**SPECIAL PRECAUTIONS:**

*Caution:*
- durvalumab can cause *immune-mediated adverse reactions*, including pneumonitis, myocarditis, hepatitis, colitis, nephritis, and various endocrinopathies, etc.; management of these reactions may require temporary durvalumab treatment interruption, administration of corticosteroids, and/or other symptomatic treatment

**SIDE EFFECTS:**

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials. When placebo-controlled trials are available, adverse events will generally be included if the incidence is ≥5% higher in the treatment group.

<table>
<thead>
<tr>
<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>gastrointestinal</td>
<td><em>emetogenic potential: none</em>¹</td>
</tr>
<tr>
<td></td>
<td>abdominal pain (10%, severe &lt;1)</td>
</tr>
<tr>
<td></td>
<td>constipation (12-25%, severe 2%)</td>
</tr>
<tr>
<td></td>
<td>nausea (7-22%, severe 2%)</td>
</tr>
<tr>
<td></td>
<td>vomiting (3-13%, severe 2%)</td>
</tr>
<tr>
<td>general disorders and administration site</td>
<td><em>extravasation hazard: none</em>³</td>
</tr>
<tr>
<td></td>
<td>edema, peripheral (8%)</td>
</tr>
<tr>
<td>ORGAN SITE</td>
<td>SIDE EFFECT</td>
</tr>
<tr>
<td>------------</td>
<td>-------------</td>
</tr>
</tbody>
</table>
| conditions | **fatigue**, asthenia (7-36%, severe 3%)  
infusion related reactions (2%, severe <1%); see paragraph following Side Effects table  
pyrexia (7-15%, severe <1%) |
| immune system (see paragraph following Side Effects table) | immune-mediated adrenal insufficiency (<1%; severe <1%); median onset 141 days  
immune-mediated myocarditis (<1%, severe <1%)  
immune-mediated colitis (2%, severe 1%); median onset 74 days  
immune-mediated diabetes mellitus, type I (<1%; severe <1%); median onset 42 days  
**immune-mediated diarrhea** (2-10%, severe 0%); median onset 74 days  
immune-mediated hepatitis (1-2%, severe 1%); median onset 70 days  
immune-mediated hyperthyroidism (1-8%, severe 0%); median onset 41 days  
immune-mediated hypophysitis/hypopituitarism (<1%; severe <1%)  
immune-mediated hypothyroidism (5-12%, severe <1%); median onset 85-107 days  
immune-mediated nephritis (<1%, severe <1%); median onset 95 days  
**immune-mediated pneumonitis** (34%, severe 1-5%); median onset 53 days  
**immune-mediated rash**, dermatitis (7-22%, severe 7%); median onset 36-74 days |
| infections and infestations (see paragraph following Side Effects table) | **pneumonia** (13-17%, severe 4-7%)  
sepsis (3%)  
upper respiratory tract infections (7-26%, severe <1%)  
**urinary tract infection** (4-16%, severe 4%) |
| investigations | **ALT increase** (8-39%, severe 1-2%)  
**AST increase** (6-36%, severe 2-4%)  
bilirubin (10%, severe 2%)  
**creatinine increase** (5-31%, severe 2%)  
hyperglycemia (44%, severe 4%)  
thyroid stimulating hormone decrease (32%)  
thyroid stimulation hormone increase (27%) |
| metabolism and nutrition | appetite decrease (8-14%) |
| musculoskeletal and connective tissue | arthralgia (7-12%, severe <1%)  
**back pain** (5-17%, severe 4%)  
myositis (<1%, severe 0%) |
| renal and urinary | **acute kidney injury** (5%, severe 2-5%) |
| respiratory, thoracic and mediastinal | dysuria (2%)  
cough (12-40%, severe <1%)  
dysphonia (4%) |
**Clinically important side effects are in bold, italics**

<table>
<thead>
<tr>
<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>dyspnea (12-22%, severe 2%)</td>
<td></td>
</tr>
<tr>
<td>skin and subcutaneous tissue</td>
<td>pruritus (7-12%, severe 5%)</td>
</tr>
</tbody>
</table>

Adapted from standard reference\(^1\)\(^2\)\(^5\)\(^6\) unless specified otherwise.

Durvalumab is generally well tolerated. The most common treatment-related adverse events are diarrhea, pneumonitis, rash, pruritus, fatigue, and decreased appetite. The majority of reactions are grade 1 or 2 and reversible with treatment interruption or administration of steroids. Events which are grade 3 or higher are infrequent.\(^1\)\(^2\)\(^5\)\(^6\) The events which are most commonly reported to lead to dose interruption or delay include pneumonia, pneumonitis, back pain, urinary tract infection, acute kidney injury, elevated liver function tests, and general health deterioration.\(^2\)

**Immune-mediated adverse events** are a spectrum of side effects caused by general immunologic enhancement that can occur at any time during durvalumab treatment. Early identification and timely intervention are important. Management of symptoms is based on the severity of the reaction and may require treatment interruption, administration of corticosteroids, and/or supportive care. If there is no improvement within 3-5 days despite steroids, consider using additional immunosuppressive therapy. Corticosteroids should be appropriately tapered following resolution of symptoms to grade 1 or less. Durvalumab may be restarted once the steroid dose has been reduced to 10 mg/day or less of prednisone (or equivalent). Referral to appropriate medical specialty may be required to manage other immune-mediated complications related to treatment. Most immune-mediated endocrinopathies can be managed by withholding durvalumab until the patient is clinically stable and/or initiating symptomatic management as indicated (e.g., insulin, thyroid hormone replacement, etc.). **Permanent discontinuation** of durvalumab should be considered for the following:

- grade 3-4: pneumonitis, hepatitis, colitis, nephritis, myocarditis, infusion-related reactions;
- grade 4: myositis, rash;
- signs of respiratory insufficiency;
- reactions which do not resolve (to grade 1 or less) within 30 days.\(^2\)

**Infusion related reactions** are reported in up to 2% of patients. Severe reactions (i.e., grade 3 or higher) have sometimes occurred. For grade 1 or 2 reactions, decrease the durvalumab infusion rate to 50% or temporarily interrupt the infusion until the reaction has resolved. Consider premedication for subsequent infusions. Permanently discontinue durvalumab for grade 3 or 4 reactions.\(^1\)\(^2\)\(^5\)

Upper respiratory tract infection, pneumonia, and urinary tract infection are the most commonly reported infections with durvalumab treatment. However, severe infections such as sepsis, necrotizing fasciitis, and osteomyelitis have also been reported. Treat as indicated. Withhold durvalumab for severe infections.\(^2\)

**INTERACTIONS:** none known\(^2\)

**SUPPLY AND STORAGE:**

**Injection:** AstraZeneca Canada Inc. supplies durvalumab as 120 mg and 500 mg ready-to-use, single-use (preservative free) vials in a concentration of 50 mg/mL. Refrigerate. Protect from light. Do not shake.\(^2\)

For basic information on the current brand used at BC Cancer, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.
SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

Additional information:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

<table>
<thead>
<tr>
<th>Method</th>
<th>BC Cancer administration guideline noted in bold, italics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous</td>
<td>no information found</td>
</tr>
<tr>
<td>Intramuscular</td>
<td>no information found</td>
</tr>
<tr>
<td>Direct intravenous</td>
<td>do NOT use</td>
</tr>
<tr>
<td>Intermittent infusion</td>
<td>over 60 minutes; use 0.2-0.22 micron inline filter to administer</td>
</tr>
<tr>
<td>Continuous infusion</td>
<td>no information found</td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>no information found</td>
</tr>
<tr>
<td>Intrapleural</td>
<td>no information found</td>
</tr>
<tr>
<td>Intrathecal</td>
<td>no information found</td>
</tr>
<tr>
<td>Intra-arterial</td>
<td>no information found</td>
</tr>
<tr>
<td>Intravesical</td>
<td>no information found</td>
</tr>
</tbody>
</table>

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:

<table>
<thead>
<tr>
<th>Method</th>
<th>Cycle Length:</th>
<th>Dose Escalation or Reduction</th>
<th>Temporarily Withhold or Permanently Discontinue Treatment if Necessary for Tolerability and/or Patient Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous</td>
<td>2 weeks&lt;sup&gt;1&lt;/sup&gt;,&lt;sup&gt;2&lt;/sup&gt;,&lt;sup&gt;6&lt;/sup&gt;</td>
<td>10 mg/kg IV for one dose on day 1 (total dose per cycle 10 mg/kg)</td>
<td></td>
</tr>
</tbody>
</table>

REFERENCES: