DRUG NAME: Cemiplimab

SYNONYM(S): cemiplimab-rwlc; REGN 2810

COMMON TRADE NAME(S): LIBTAYO® (USA)

CLASSIFICATION: immunotherapy

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

MECHANISM OF ACTION:

Cemiplimab is a recombinant human IgG monoclonal antibody immune checkpoint inhibitor that binds to programmed death receptor-1 (PD-1) on T cells and blocks the interaction with its ligands, PD-L1 and PD-L2. Inhibition of the receptor/ligand signalling restores the anti-tumour immune response. In animal models, blocking PD-1 activity resulted in decreased tumour growth.

USES:

Primary uses:
Skin cancer, squamous cell

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:

Contraindications:
• history of hypersensitivity reaction to cemiplimab or Chinese hamster ovary cell proteins

Caution:
• based on its mechanism of action, cemiplimab can cause fetal harm when administered to a pregnant woman; females of reproductive potential should use effective contraception during treatment and for at least 4 months after the last dose

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>blood and lymphatic system/ febrile neutropenia</td>
<td>anemia (severe 2%)</td>
</tr>
<tr>
<td></td>
<td>lymphopenia (severe 7%)</td>
</tr>
<tr>
<td>cardiac</td>
<td>immune-mediated myocarditis, pericarditis (&lt;1%)</td>
</tr>
<tr>
<td>endocrine</td>
<td>immune-mediated adrenal insufficiency (&lt;1%, severe &lt;1%)</td>
</tr>
<tr>
<td></td>
<td><strong>immune-mediated type I diabetes mellitus</strong> (1%, severe 1%); may present with ketoacidosis</td>
</tr>
</tbody>
</table>

Clinically important side effects are in **bold, italics**
<table>
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<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
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</thead>
</table>
| Clinically important side effects are in **bold, italics**

**immune-mediated hyperthyroidism** (2%, severe <1%)
immune-mediated hypophysitis (<1%, severe <1%)
**immune-mediated hypothyroidism** (6%, severe <1%)

**eye** (see paragraph following Side Effects table)
**immune-mediated iritis** (<1%)
immune-mediated ocular inflammation (<1%)
**immune-mediated uveitis** (<1%)

**gastrointestinal**
*emetogenic potential: minimal*
constipation (12%, severe <1%)
**diarrhea** (22%, severe <1%)
**immune-mediated colitis** (1%, severe <1%)
immune-mediated pancreatitis (<1%)
nausea (19%)

**general disorders and administration site conditions**
extravasation hazard: none
**fatigue** (29%, severe 2%)
infusion-related reactions (severe <1%); see paragraph following Side Effects table

**hepatobiliary**
**immune-mediated hepatitis** (2%, severe 2%)

**immune system**
refer to organ site; see paragraph following Side Effects table

**infections and infestations**
cellulitis, skin infection (severe ≥2%)
pneumonia (severe ≥2%)
sepsis (severe ≥2%)
urinary tract infection (severe ≥2%)

**investigations**
AST increase (severe 3%)
hypercacemia (severe 1%)
yponatremia (severe 3%)
yhypophosphatemia (severe 4%)

**metabolism and nutrition**
appetite decrease (10%)
hypoalbuminemia (severe 1%)

**musculoskeletal and connective tissue**
immune-mediated myositis, rhabdomyolysis (<1%)
**musculoskeletal pain** (17%, severe 3%)

**nervous system**
immune-mediated aseptic meningitis (<1%)
immune-mediated Guillain-Barre syndrome (<1%)
immune-mediated myelitis and demyelination (<1%)

**renal and urinary**
immune-mediated nephritis (1%, severe <1%)

**respiratory, thoracic and mediastinal**
**immune-mediated pneumonitis** (2%, severe 1%)

**skin and subcutaneous**
erythema multiforme and pemphigoid (2%, severe 1%)
<table>
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<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>tissue</td>
<td><strong>pruritus</strong> (15%)</td>
</tr>
<tr>
<td></td>
<td><strong>rash</strong> (25%, severe 1%)</td>
</tr>
<tr>
<td></td>
<td>Stevens-Johnson syndrome (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>toxic epidermal necrolysis (&lt;1%)</td>
</tr>
<tr>
<td>vascular</td>
<td><strong>hypertension</strong> (severe ≥2%)</td>
</tr>
</tbody>
</table>

Clinically important side effects are in **bold, italics**

Adapted from standard reference unless specified otherwise.

The **most common** adverse reactions (reported incidence ≥ 20%) are fatigue, rash, and diarrhea. The most common grade 3 or 4 events (reported incidence ≥2%) are cellulitis, sepsis, hypertension, pneumonia, musculoskeletal pain, skin infection, urinary tract infection, and fatigue.

Severe **infusion-related reactions** are reported in less than 1% of patients. Depending on the severity of the reaction, reactions may be managed by interrupting or slowing the rate of infusion, although permanent discontinuation of cemiplimab may be necessary.

Cemiplimab is a programmed death receptor-1 (PD-1) inhibitor, a class of drugs which, by its mechanism, removes the inhibition of the immune response. Therefore, **immune-mediated** side effects can occur in any organ system or tissue and reactions may be severe or fatal. While immune-mediated reactions usually occur during the course of treatment, they may also manifest after the PD-1 inhibitor has been discontinued. Early identification and management of immune-mediated side effects are essential for safe use of cemiplimab. In general, cemiplimab is withheld for grade 3 or 4 reactions, and some grade 2 reactions, and permanently discontinued for grade 4 reactions. Corticosteroids are administered until reactions improve to grade 1 or less, and then tapered over one month. Other systemic immunosuppressants may be required if reactions are not controlled with corticosteroids. For symptomatic endocrinopathies, appropriate hormone therapy may be required.

Uveitis, iritis, and other immune-mediated **ocular toxicities** are rare but some cases have been associated with retinal detachment. Varying degrees of visual impairment, including blindness, can occur. Consider a diagnosis of Vogt-Koyanagi-Harada-like syndrome if uveitis occurs in combination with other immune-mediated reactions. Systemic corticosteroids may be required to reduce the risk of permanent vision loss.

**SUPPLY AND STORAGE:**

**Injection:** Regeneron Pharmaceuticals, Inc. supplies cemiplimab as 250 mg ready-to-use, single-use (preservative-free) vials in a concentration of 50 mg/mL. Refrigerate. Do not shake. Protect from light in original carton.

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>Notes</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>no information found</td>
</tr>
<tr>
<td>Intermittent infusion³</td>
<td>over 30 minutes; use 0.2 micron inline filter</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>
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<tr>
<td>Intrathecal</td>
<td>no information found</td>
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<tr>
<td>Intra-arterial</td>
<td>no information found</td>
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<tr>
<td>Intravesical</td>
<td>no information found</td>
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</tbody>
</table>

**DOSAGE GUIDELINES:**

Refer to protocol by which patient is being treated.

**Adults:**

- **Cycle Length:**
  - Intravenous:
    - **2 weeks⁷:** 3 mg/kg IV for one dose on day 1 (total dose per cycle 3 mg/kg)
    - **3 weeks¹:** 350 mg IV for one dose on day 1 (total dose per cycle 350 mg)

Dosage reductions are not recommended.¹

**REFERENCES:**

1. Regeneron Pharmaceuticals Inc. LIBTAYO® full prescribing information. Tarrytown, New York, USA; September 2018.