**DRUG NAME:** Carmustine

**SYNONYM(S):** BCNU

**COMMON TRADE NAME(S):** BiCNU®, GLIADEL® Wafer

**CLASSIFICATION:** alkylating agent

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

**MECHANISM OF ACTION:**

Carmustine is a highly lipid-soluble nitrosourea compound. Carmustine, a bifunctional alkylating agent, alkylates DNA and RNA, can cross-link DNA, and inhibits several enzymes by carbamoylation. It is cell-cycle phase nonspecific. Carmustine is generally not cross-resistant with other alkylating agents, however, cross-resistance between carmustine and lomustine has occurred.

**PHARMACOKINETICS:**

Table refers to intravenous (IV) dosing. Pharmacokinetic properties of the implantable carmustine-impregnated wafer have not been evaluated. High-dose is defined here as >200 mg/m².

| Oral Absorption | not known
| Distribution | highly lipid soluble (e.g., enters breast milk, brain)
| | cross blood brain barrier? | passes readily (15-70% of concurrent plasma concentrations)
| | volume of distribution | 3.25 L/kg (5.1 L/kg, high dose)
| | plasma protein binding | 80%
| Metabolism | rapid spontaneous decomposition; significant hepatic metabolism
| active metabolite(s) | yes
| inactive metabolite(s) | yes
| Excretion | predominately renal; respiratory 6-10% as CO₂
| urine | 60-70% within 96 h
| feces | <1%
| terminal half life | 0.25-0.75 h, non-linear dose-related
| clearance | 56 mL/min/kg (78 mL/min/kg, high dose)

Adapted from standard reference unless specified otherwise.
USES:
(Table refers to intravenous (IV) dosing except where specified.)

**Primary uses:**
- Brain tumours
- Glioma (implantable carmustine-impregnated wafer)
- Lymphoma, Hodgkin’s disease
- Lymphoma, non-Hodgkin’s
- Multiple myeloma
- Melanoma
- Gastrointestinal cancer

**Other uses:**
- Glioblastoma\textsuperscript{10} (implantable carmustine-impregnated wafer)
- Lymphoma, cutaneous T-cell\textsuperscript{1.11} (topical carmustine)

*S*Health Canada approved indication

SPECIAL PRECAUTIONS:

**Caution:**
- Dose-related *pulmonary toxicity* is reported with carmustine injection; patients receiving cumulative doses more than 1,400 mg/m\textsuperscript{2} are at higher risk. Single doses of >450 mg/m\textsuperscript{2} may be associated with the development of acute lung injury in approximately 20% of patients.\textsuperscript{7}

**Special populations:** Carmustine injection should be used with extreme caution in *children* due to the high risk of pulmonary toxicity.\textsuperscript{4}

**Carcinogenicity:** Carmustine is carcinogenic in rats and mice, producing a marked increase in tumour incidence with therapeutic doses.\textsuperscript{4}

**Mutagenicity:** Mutagenic in Ames test and mammalian *in vitro* mutation test.\textsuperscript{12} Carmustine is clastogenic in mammalian *in vitro* and *in vivo* chromosome tests.

**Fertility:** Carmustine affects fertility in male rats at doses somewhat higher than human doses.\textsuperscript{4}

**Pregnancy:** In animal studies, carmustine is embryotoxic and teratogenic at doses equivalent to human doses.\textsuperscript{13}

**Breastfeeding** is contraindicated as carmustine is detected in human breast milk.\textsuperscript{7}

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, and/or determined to be clinically important. When placebo-controlled trials are available, adverse events are included if the incidence is $\geq 5\%$ higher in the treatment group.
CARMUSTINE INJECTION:
High-dose is defined here as >200 mg/m².

<table>
<thead>
<tr>
<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>blood/bone marrow/febrile neutropenia</td>
<td>anemia (1-10%)&lt;sup&gt;7&lt;/sup&gt; myelosuppression (&gt;10%)&lt;sup&gt;7&lt;/sup&gt;; onset 7-14 days, nadir 21-35 days, recovery 42-56 days; cumulative, dose related, delayed and often biphasic&lt;sup&gt;10&lt;/sup&gt;; see paragraph following Side Effects table</td>
</tr>
<tr>
<td>cardiovascular (general)</td>
<td>hypotension, due to alcohol content of diluent (high-dose therapy &gt;10%)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>dermatology/skin</td>
<td>alopecia&lt;sup&gt;8&lt;/sup&gt; (1-10%)&lt;sup&gt;7&lt;/sup&gt; dermatitis with topical use (50%)&lt;sup&gt;9&lt;/sup&gt; improves with reduced concentration of compounded product flushing, due to alcohol content of diluent (1-10%)&lt;sup&gt;7&lt;/sup&gt;; increased with administration times &lt;1-2 h&lt;sup&gt;16&lt;/sup&gt; hyperpigmentation, transient, with accidental skin contact (&gt;10%)&lt;sup&gt;7&lt;/sup&gt; injection site reaction; see paragraph following Side Effects table</td>
</tr>
<tr>
<td>gastrointestinal</td>
<td>emetogenic potential&lt;sup&gt;17&lt;/sup&gt;; &gt;250 mg/m² high; &lt;250 mg/m² high-moderate anorexia (1-10%)&lt;sup&gt;7&lt;/sup&gt; constipation (1-10%)&lt;sup&gt;7&lt;/sup&gt; diarrhea (1-10%)&lt;sup&gt;7&lt;/sup&gt; nausea and vomiting (severe &gt;10%)&lt;sup&gt;7&lt;/sup&gt;; begins within 2-4 h of administration and lasts for 4-6 h stomatitis (1-10%)</td>
</tr>
<tr>
<td>hepatobiliary/pancreas</td>
<td>hepatotoxicity, reversible, delayed up to 60 days after administration (&lt;1%, high-dose therapy 1-10 % and dose-limiting&lt;sup&gt;10&lt;/sup&gt;)</td>
</tr>
<tr>
<td>metabolic/laboratory</td>
<td>alkaline phosphatase, reversible increase (&gt;20-25%)&lt;sup&gt;7&lt;/sup&gt; bilirubin, reversible increase (&gt;20-25%)&lt;sup&gt;7&lt;/sup&gt; SGOT, reversible increase (&gt;20-25%)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>neurology</td>
<td>ataxia (&gt;10%)&lt;sup&gt;7&lt;/sup&gt; dizziness (&gt;10%)&lt;sup&gt;7&lt;/sup&gt; encephalopathy (&lt;1%, high-dose therapy 1-10% and dose-limiting&lt;sup&gt;10&lt;/sup&gt;)</td>
</tr>
<tr>
<td>ocular/visual</td>
<td>ocular toxicities, transient conjunctival flushing and blurred vision; retinal hemorrhages (&gt;10%)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>pain</td>
<td>headache&lt;sup&gt;1&lt;/sup&gt; muscular pain (&lt;1%)</td>
</tr>
<tr>
<td>pulmonary</td>
<td>pulmonary toxicity (up to 30%); see paragraph following Side Effects table BCNU pneumonitis&lt;sup&gt;18&lt;/sup&gt; (20% for doses &gt;450 mg/m²)&lt;sup&gt;18&lt;/sup&gt;; see paragraph following Side Effects table interstitial fibrosis (&lt;1%, up to 50% for cumulative doses &gt;1,400 mg/m²)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>renal/genitourinary</td>
<td>renal toxicity&lt;sup&gt;6&lt;/sup&gt;&lt;sup&gt;,10&lt;/sup&gt; (&lt;1% for cumulative doses &lt;1,000 mg/m²)</td>
</tr>
</tbody>
</table>

Developed: September 1994
Revised: 1 May 2022
### Carmustine

<table>
<thead>
<tr>
<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>secondary malignancy</td>
<td>acute leukemias, bone marrow dysplasias&lt;sup&gt;4&lt;/sup&gt;; following long-term use</td>
</tr>
<tr>
<td>sexual/reproductive function</td>
<td>gynecomastia (&lt;1%)&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>infertility&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>teratogenesis&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>vascular</td>
<td>phlebitis (&gt;10%)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>veno-occlusive disease&lt;sup&gt;6&lt;/sup&gt; (high-dose therapy &lt;1%)&lt;sup&gt;10&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Adapted from standard reference<sup>4</sup> unless specified otherwise.

### IMPLANTABLE CARMUSTINE-IMPREGNATED WAFER:

<table>
<thead>
<tr>
<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>allergy/immunology</td>
<td>allergic reaction (1%)</td>
</tr>
<tr>
<td>cardiovascular (arrhythmia)</td>
<td>tachycardia (2%)</td>
</tr>
<tr>
<td>cardiovascular (general)</td>
<td>hypertension (3%)</td>
</tr>
<tr>
<td></td>
<td>hypotension (3%)</td>
</tr>
<tr>
<td>constitutional symptoms</td>
<td>accidental injury (1-5%)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>aggravation reaction, defined as progression of tumour or disease or general deterioration (82%)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>asthenia (1%)</td>
</tr>
<tr>
<td></td>
<td>insomnia (1-10%)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>dermatology/skin</td>
<td>alopecia does not occur&lt;sup&gt;19&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>wound healing complications, at site of implantation,&lt;sup&gt;20&lt;/sup&gt; including cerebrospinal fluid leaks, subdural fluid collection and wound healing (12%)</td>
</tr>
<tr>
<td>endocrine</td>
<td>Cushing’s syndrome (3%)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>diabetes mellitus (5%)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>gastrointestinal</td>
<td>emetogenic potential: rare</td>
</tr>
<tr>
<td></td>
<td>constipation (1%)</td>
</tr>
<tr>
<td></td>
<td>dysphagia (1%)</td>
</tr>
<tr>
<td></td>
<td>vomiting (2%)</td>
</tr>
<tr>
<td>hemorrhage</td>
<td>hemorrhage, gastrointestinal (1%)</td>
</tr>
<tr>
<td>infection</td>
<td>intracranial infection, meningitis, or abscess&lt;sup&gt;6&lt;/sup&gt;(1-10%)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>oral moniliasis (3%)</td>
</tr>
<tr>
<td>lymphatics</td>
<td>edema, cerebral (1-10%)&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>edema, peripheral (3%)</td>
</tr>
</tbody>
</table>
### Carmustine

**ORGAN SITE** | **SIDE EFFECT**
--- | ---
metabolic/laboratory | hyponatremia (3%)
 | hypokalemia (1%)
 | hyperglycemia (2%)

**neurology**<sup>7</sup> | **brain swelling**: amnesia (1-10%); aphasia (1-10%); ataxia (1-10%); confusion (1-10%); convulsion (1-10%); dizziness (1-10%); hemiplegia (1-10%); hydrocephalus (1-10%); monoplegia (2%); seizures (> 10%): somnolence (1-10%); stupor (1-10%); abnormal thinking (3%)

**ocular/visual** | diplopia (1-10%)<sup>7</sup>

**pain** | chest pain (1%)
 | headache (1-10%)<sup>7</sup>
 | pain (4%)

**renal/genitourinary** | urinary incontinence (2%)

**vascular** | phlebitis (10%)<sup>1</sup>
 | pulmonary embolism (4-8%, at initial surgery)<sup>1</sup>

Adapted from standard reference<sup>5</sup> unless specified otherwise.

### TOPICAL CARMUSTINE:

**ORGAN SITE** | **SIDE EFFECT**
--- | ---
blood and lymphatic system/ febrile neutropenia | leucopenia (4-10%)<sup>21-23</sup>; mild, possibly higher incidence with solution versus ointment and with greater surface area treated
 | anemia; mild

skin and subcutaneous tissue | dermatitis (<10%); allergic or irritant
 | erythema (>50%); see paragraph following Side Effects table
 | telangiectasia

Adapted from standard reference<sup>21</sup> unless specified otherwise.

**Erythema** is experienced by the majority of patients following topical carmustine, particularly with the compounded solution. Erythema is often accompanied by a burning sensation, likened to sunburn, and skin tenderness.<sup>21,23</sup> The reaction may manifest as hyperpigmentation in individuals with dark hair or dark complexions.<sup>22,24</sup> Erythema tends to be accentuated in body folds, the groin area, and axillae.<sup>21</sup> With total body applications, reactions usually appear within 4-8 weeks.<sup>22,23</sup> Reactions may require treatment with intensive topical corticosteroids, cool compresses or baths, and emollients. In severe, and sometimes even moderate erythematous reactions, the reaction may be followed by a benign telangiectasia. Telangiectasia usually involutes within a few months, but in severe cases may persist for years before gradually resolving. Secondary skin cancers were not reported.<sup>21,23,25</sup>

Rapid IV infusion may result in **flushing of the skin and conjunctiva**, likely due to the alcohol diluent. These effects can occur within 2 hours and may continue for 4 hours after administration of carmustine. Infusions should run over 1-2 hours. For high-dose carmustine, the maximum rate is 3 mg/m²/min to avoid excessive flushing, agitation, and hypotension.<sup>7</sup>
Burning and hyperemia at the injection site, or along the course of the vein, are common during carmustine injection. Vasospasm is also common, but thrombosis and thrombophlebitis are rare.

Delayed myelosuppression occurs frequently with carmustine injection, and may be severe. This is cumulative and usually occurs 4-6 weeks after administration of the drug. Thrombocytopenia is generally greater than leukopenia; however, both may be dose-limiting toxicities. Anemia also occurs but is generally less severe. Due to the delayed and cumulative myelosuppressive effects, carmustine is usually given at intervals of at least 6 weeks. However, repeat courses of carmustine should not be administered until leukocyte and platelet counts have returned to acceptable levels.

Pulmonary fibrosis and pulmonary infiltrates can occur with carmustine injection. Pulmonary toxicities are more common with prolonged therapy and with cumulative doses >1,400 mg/m²; however, pulmonary toxicity has occurred with lower doses. Early-onset pulmonary toxicity appears within 3 years of therapy (9 days to 43 months); however, late-onset pulmonary fibrosis has been reported up to 17 years after treatment. Risk factors include smoking, pre-existing respiratory condition(s), sequential or concomitant thoracic irradiation, and the use of other drugs that cause lung damage. Monitor pulmonary function tests at baseline and throughout treatment. Patients should be advised to immediately report any signs of respiratory complications, and this should result in discontinuation of therapy. Note that carmustine therapy during childhood may result in asymptomatic lung fibrosis that may become symptomatic in adulthood.

Unlike pulmonary fibrosis, BCNU pneumonitis (also known as BCNU lung or idiopathic pneumonia syndrome) may occur following a single dose or course of therapy. BCNU pneumonitis requires emergency treatment as it is potentially fatal. Patients typically present 30-100 days after autologous BMT with fever, cough, dyspnea and pulmonary infiltrates on x-ray. Risk factors include those identified for pulmonary fibrosis, as well as female sex. It has been suggested that doses less than 475 mg/m² may reduce the risk, particularly in females. However, BCNU pneumonitis is also reported at lower doses (e.g., 300 mg/m²). Treatment includes high-dose prednisone, as well as antibiotics if pneumonia is suspected.

INTERACTIONS:

Table refers to IV administration only. Interactions with the implantable carmustine-impregnated wafer and compounded topical formulation have not been evaluated.

<table>
<thead>
<tr>
<th>AGENT</th>
<th>EFFECT</th>
<th>MECHANISM</th>
<th>MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>cimetidine</td>
<td>delayed, major, suspected; increased carmustine toxic effect</td>
<td>possible inhibition of carmustine metabolism</td>
<td>avoid concomitant use</td>
</tr>
<tr>
<td>digoxin tablets</td>
<td>delayed, moderate, suspected; decreased effect of digoxin</td>
<td>changes to intestinal mucosa may decrease digoxin absorption</td>
<td>consider monitoring digoxin levels; adjust digoxin dose as needed</td>
</tr>
<tr>
<td>melphalan</td>
<td>increased risk of pulmonary toxicity</td>
<td>melphalan may reduce the threshold for carmustine-induced pulmonary toxicity</td>
<td>caution; monitor for pulmonary toxicity</td>
</tr>
<tr>
<td>phenytoin</td>
<td>delayed, moderate, suspected; decreased phenytoin levels</td>
<td>decreased absorption or increased metabolism of phenytoin</td>
<td>monitor serum phenytoin levels during and after carmustine therapy; adjust phenytoin dose as needed</td>
</tr>
</tbody>
</table>

SUPPLY AND STORAGE:

Injection: Marcan Pharmaceuticals Inc. supplies carmustine as 100 mg vials of lyophilized powder. Store in fridge. Diluent (anhydrous ethanol) is supplied separately in a 3 mL vial.
**Additional information:**
- Carmustine powder should appear as dry flakes or a dry, rigid mass. Carmustine has a low melting point and is subject to liquefaction at temperatures greater than 27 ºC. Discard if oily film is present as this is a sign of disintegration.\(^\text{13}\)

**Wafer:** Arbor Pharmaceuticals LLC supplies carmustine in a polifeprosan wafer. It is available in a single-dose treatment box containing eight individually pouched wafers. Each wafer contains 7.7 mg (3.85%) of carmustine. Each wafer is packaged in two aluminum foil laminate pouches. The inner pouch is sterile and maintains the sterility of the wafer. The second pouch is a peelable overwrap. The aluminum foil pouches containing GLIADEL® should be delivered to the operating room and remain unopened until ready to implant the wafers. The product must be stored at or below -20ºC. Unopened foil pouches may be kept at ambient room temperature for a maximum of six hours.\(^\text{5}\)

*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 for carmustine injection:**
- accidental contact of carmustine with the skin has caused burns and excessive pigmentation in affected areas\(^\text{13}\)
- to facilitate mixing, allow powder and supplied diluent (anhydrous alcohol) to come to room temperature prior to mixing\(^\text{13}\)
- precipitation may occur following refrigeration of the reconstituted solution; precipitates may be dissolved by warming the vial to room temperature and gently shaking\(^\text{13}\)
- diluted carmustine is unstable in PVC containers; use glass or polypropylene containers for preparation\(^\text{13}\)
- alternative reconstitution directions have been suggested to minimize the volume of ethanol used; however, there is limited evidence to support their clinical use\(^\text{37-40}\)
- protect diluted carmustine from light during storage and administration\(^\text{13}\)
- prior to administration, final product should be gently shaken for ~10 sec to remix bag contents\(^\text{13}\)
- administer carmustine using non-PVC administration sets\(^\text{13}\)

**Additional information for topical carmustine ointment:**
To yield a 0.4% ointment in white petrolatum:
- Reconstitute each 100 mg carmustine vial with 3 mL absolute alcohol (supplied diluent) to give 33.3 mg/mL. Shake to dissolve.
- Withdraw vial contents and mix with 25 g of white petrolatum per vial.\(^\text{24}\)
The final product is stable for 6 months in the refrigerator\(^\text{23}\) or 3 months at room temperature.\(^\text{24}\) A change in colour to brown indicates occurrence of oxidation, and the ointment should be discarded.\(^\text{23}\)

### PARENTERAL ADMINISTRATION:

<table>
<thead>
<tr>
<th>Method</th>
<th>BC Cancer administration guideline noted in <strong>bold, italics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous</td>
<td>not used due to corrosive nature</td>
</tr>
<tr>
<td>Intramuscular</td>
<td>not used due to corrosive nature</td>
</tr>
<tr>
<td>Intratumourial</td>
<td>implantable carmustine-impregnated wafer</td>
</tr>
<tr>
<td>Direct intravenous</td>
<td>no information found</td>
</tr>
<tr>
<td><strong>Intermittent infusion</strong></td>
<td>over 1-2 h; administer using non-PVC administration set(^\text{13})</td>
</tr>
<tr>
<td>Continuous infusion</td>
<td>not used due to corrosive nature</td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>no information found</td>
</tr>
</tbody>
</table>
Carmustine

<table>
<thead>
<tr>
<th>Administration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrapleural</td>
<td>not used due to corrosive nature</td>
</tr>
<tr>
<td>Intrathecal</td>
<td>not used due to corrosive nature</td>
</tr>
<tr>
<td>Intra-arterial</td>
<td>has been used⁴</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>Cycle Length</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intravenous:</strong></td>
<td></td>
</tr>
<tr>
<td>4-6 weeks⁷</td>
<td>20-65 mg/m² (0.5-1 mg/kg) IV for one dose on day 1 (total dose per cycle 20-65 mg/m² [0.5-1 mg/kg])</td>
</tr>
<tr>
<td>6 weeks⁴¹</td>
<td>100 mg/m² IV for one dose on day 1 for 3-6 cycles (total dose per cycle 100 mg/m²)</td>
</tr>
<tr>
<td>6-8 weeks⁷</td>
<td>150-200 mg/m² IV once daily as a single dose on day 1, or divided into daily injections on 2 consecutive days starting on day 1 (total dose per cycle 150-200 mg/m²)</td>
</tr>
<tr>
<td>6-8 weeks⁷</td>
<td>75-120 mg/m² IV once daily for 2 consecutive days starting on day 1 (total dose per cycle 150-240 mg/m²)</td>
</tr>
<tr>
<td>6-8 weeks⁷</td>
<td>40-80 mg/m² IV once daily for three consecutive days starting on day 1 (total dose per cycle 120-240 mg/m²)</td>
</tr>
<tr>
<td><strong>Bone marrow transplant⁴²,⁴³:</strong></td>
<td>combination therapy: 500 mg/m² IV for one dose (on day -2) (total dose 500 mg/m²) Note: these doses are fatal without bone marrow/stem cell transplant.</td>
</tr>
<tr>
<td><strong>Bone marrow transplant⁴⁴:</strong></td>
<td>combination therapy: 300 mg/m² IV for one dose (on day -6) (total dose 300 mg/m²) Note: these doses are fatal without bone marrow/stem cell transplant.</td>
</tr>
</tbody>
</table>
Intratumoural:

Cycle Length: n/a:

Implantation: up to 8 wafers placed in the resection cavity (total dose 61.6 mg); if the size and shape does not accommodate 8 wafers, the maximum number of wafers allowed should be placed.

In patients undergoing surgery and intracranial implantation of carmustine wafers for recurrent malignant glioma, chemotherapy is held for at least 4 weeks (6 weeks for nitrosoureas) prior to and 2 weeks after surgery.\(^1,5\)

Topical:

Cycle Length: n/a:

0.4% ointment in white petrolatum applied once daily to individual lesions or regional areas.\(^21-23,45\)

Rub into skin surface to apply and wash off after 6-8 hours with soap and water\(^23\).

OR

n/a:

10 mg daily (as an alcoholic solution or ointment) usually applied once daily for 7-14 weeks (maximum 17 weeks). If inadequate response, a second course of topical therapy is administered after a rest interval of 6 weeks, using 20 mg daily for 4-8 weeks, as tolerated.\(^1,11\)

Concurrent radiation:

- carmustine injection\(^14\): consolidation irradiation may be required to residual masses post-transplant after count recovery and overall improvement
- implantable carmustine-impregnated wafer\(^5\): external beam radiation initiated no sooner than 3 weeks after implantation

Dosage in myelosuppression:

modify according to protocol by which patient is being treated; suggested dose modification\(^41\) (NOT to be used for BMT dosing)

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose (as percentage of prior dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.5</td>
<td>&gt;125</td>
<td>100%</td>
</tr>
<tr>
<td>1-1.5</td>
<td>100-125</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;1</td>
<td>&lt;100</td>
<td>omit</td>
</tr>
</tbody>
</table>

Dosage in renal failure\(^46\):

GFR <10 mL/min: discontinue

calculated creatinine clearance = \(N \times (140 - \text{Age}) \times \text{weight in kg} \div \text{serum creatinine in micromol/L}\)

* For males \(N=1.23\); for females \(N=1.04\)

Dosage in hepatic failure\(^3\):

no information found; dosage adjustment may be necessary based on liver function test results

Dosage in dialysis:

no information found
Children:

Intravenous:

Cycle Length: 4-6 week

200-250 mg/m² IV for one dose on day 1 (total dose per cycle 200-250 mg/m²)

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44. Leukemia/Bone Marrow Transplantation Program of British Columbia. (BMTBEAM) Intensive Therapy and Autografting for Progressive Hodgkin's Disease or Progressive Non-Hodgkin's Lymphoma. Vancouver, British Columbia: BC Cancer Agency; 10 May 2004