

## Prior Authorization DRUG Guidelines

### **Bicnu (carmustine)**

Effective Date: 10/22/13

Date Developed: 9/3/13 by Albert Reeves MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20,  
8/3/21, 2/1/22, 1/31/23, 2/13/24, 2/18/25

**Pharmacologic Category:** Antineoplastic Agent; Alkylating Agent (Nitrosourea)

#### Preauthorization Criteria:

**Injection:** Palliative treatment: brain tumors (glioblastoma, brainstem glioma, medulloblastoma, astrocytoma, ependymoma, and metastatic brain tumors), multiple myeloma, Hodgkin's lymphoma (relapsed or refractory), non-Hodgkin's lymphomas (relapsed or refractory)

**Wafer (implant):** Adjunct to surgery in patients with recurrent glioblastoma multiforme; adjunct to surgery and radiation in patients with newly diagnosed high-grade malignant glioma

**Off-Label:** Hematopoietic cell or bone marrow transplant, autologous, conditioning regimen; Mycosis fungoides, early stage (topical)

#### Dosing:

**NOTE:** Carmustine (IV) is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting

**NOTE:** Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.

**NOTE:** Consult current product information for potential updates.

**NOTE:** Utilize patient's actual body weight (full weight) for calculation of body surface area or weight-based dosing in obese patients (refer to ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer)

**Adult: Brain tumors, Hodgkin's lymphoma, multiple myeloma, non-Hodgkin's lymphoma (per manufacturer labeling):** I.V.: 150-200 mg/m<sup>2</sup> every 6 weeks or 75-100 mg/m<sup>2</sup>/day for 2 days every 6 weeks

**Glioblastoma multiforme (recurrent), newly diagnosed high-grade malignant glioma:**  
Implantation (wafer): 8 wafers placed in the resection cavity (total dose 61.6 mg); should the size and shape not accommodate 8 wafers, the maximum number of wafers allowed (up to 8) should be placed

**Indication-specific dosing:**

**Brain tumor, primary (unlabeled doses): I.V.:**

80 mg/m<sup>2</sup>/day for 3 days every 8 weeks for 6 cycles (Brandes, 2004)

200 mg/m<sup>2</sup> every 8 weeks [maximum cumulative dose: 1500 mg/m<sup>2</sup>] (Selker, 2002)

**Hodgkin's lymphoma, relapsed or refractory (unlabeled dose): I.V.: Mini-BEAM regimen:**

60 mg/m<sup>2</sup> day 1 every 4-6 weeks (in combination with etoposide, cytarabine, and melphalan) (Colwill, 1995; Martin, 2001)

**Multiple myeloma, relapsed, refractory (unlabeled dose): I.V.: VBMCP regimen: 20 mg/m<sup>2</sup>**

day 1 every 35 days (in combination with vincristine, melphalan, cyclophosphamide, and prednisone) (Kyle, 2006; Oken, 1997)

**Mycosis fungoides, early stage (unlabeled use; Zackheim, 2003): Topical:**

Ointment (10 mg/100 grams petrolatum): Apply (with gloves) once daily to affected areas

Solution (0.2% solution in alcohol; dilute 5 mL in 60 mL water): Apply (with gloves) once daily to affected areas

**Stem cell or bone marrow transplant, autologous (unlabeled use): I.V.:**

BEAM regimen: 300 mg/m<sup>2</sup> 6 days prior to transplant (in combination with etoposide, cytarabine, and melphalan) (Chopra, 1993; Linch, 2010)

CBV regimen: 600 mg/m<sup>2</sup> 3 days prior to transplant (in combination with cyclophosphamide and etoposide) (Reece, 1991)

## **Dosing: Geriatric**

Refer to adult dosing.

## **Dosing: Renal Impairment**

I.V.: The FDA-approved labeling does not contain renal dosing adjustment guidelines. The following dosage adjustments have been used by some clinicians (Kintzel, 1995):

Cl<sub>cr</sub> 46-60 mL/minute: Administer 80% of dose

Cl<sub>cr</sub> 31-45 mL/minute: Administer 75% of dose

Cl<sub>cr</sub> ≤30 mL/minute: Consider use of alternative drug.

## **Dosing: Hepatic Impairment**

Dosage adjustment may be necessary; however, no specific guidelines are available.

resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

## Dosing: Adjustment for Toxicity

**Hematologic toxicity:** Based on nadir counts with previous dose (manufacturer's labeling). I.V.:

If leukocytes  $>3000/\text{mm}^3$  and platelets  $>75,000/\text{mm}^3$ : Administer 100% of dose

If leukocytes  $2000\text{--}2999/\text{mm}^3$  or platelets  $25,000\text{--}74,999/\text{mm}^3$ : Administer 70% of dose

If leukocytes  $<2000/\text{mm}^3$  or platelets  $<25,000/\text{mm}^3$ : Administer 50% of dose

## Major Adverse Reactions and Black Box Warnings: I.V.: Frequency not defined:

Cardiovascular: Arrhythmia (with high doses), chest pain, flushing (with rapid infusion), hypotension, tachycardia

Central nervous system: Ataxia, dizziness

Central nervous system: Ethanol intoxication (with high doses), headache

Dermatologic: Hyperpigmentation/skin burning (after skin contact)

Gastrointestinal: Nausea (common; dose related), vomiting (common; dose related), mucositis (with high doses), toxic enterocolitis (with high doses)

Hematologic: Leukopenia (common; onset: 5-6 weeks; recovery: after 1-2 weeks), thrombocytopenia (common: onset: ~4 weeks; recovery: after 1-2 weeks), anemia, neutropenic fever, secondary malignancies (acute leukemia, bone marrow dysplasia)

Hepatic: Alkaline phosphatase increased, bilirubin increased, hepatic sinusoidal obstruction syndrome (SOS; veno-occlusive disease; with high doses), transaminases increased

Local: Injection site reactions (burning, erythema, necrosis, pain, swelling)

Ocular: Conjunctival suffusion (with rapid infusion), neuroretinitis

Renal: Kidney size decreased, progressive azotemia, renal failure

Respiratory: Interstitial pneumonitis (with high doses), pulmonary fibrosis, pulmonary hypoplasia, pulmonary infiltrates

Miscellaneous: Allergic reaction, infection (with high doses)

## Wafer:

$\geq 4\%$  (percentages reported only where incidence was greater compared to placebo):

Cardiovascular: Deep thrombophlebitis (10%), facial edema (6%), chest pain (5%)

Central nervous system: Brain edema (4% to 23%), confusion (10% to 23%), depression (16%), headache (15%), somnolence (14%), fever (12%), speech disorder (11%),

intracranial hypertension (9%), anxiety (7%), facial paralysis (7%), pain (7%), ataxia (6%), hypesthesia (6%), hallucination (5%), seizure (grand mal 5%), meningitis (4%)

Dermatologic: Abnormal wound healing (14% to 16%), rash (5% to 12%)

Endocrine: Diabetes (5%)

Gastrointestinal: Nausea (8% to 22%), vomiting (8% to 21%), constipation (19%), abdominal pain (8%), diarrhea (5%)

Genitourinary: Urinary tract infection (21%)

Hematologic: Hemorrhage (7%)

Local: Abscess (4% to 8%)

Neuromuscular & skeletal: Weakness (22%), back pain (7%)

## Contraindications

Hypersensitivity to carmustine or any component of the formulation

## BOXED WARNINGS:

**Bone marrow suppression (primarily thrombocytopenia and leukopenia) is the major carmustine toxicity; generally, is delayed.** Monitor blood counts weekly for at least 6 weeks after administration. Myelosuppression is cumulative. When given at the FDA-approved doses, treatment should not be administered less than 6 weeks apart. Consider nadir blood counts from prior dose for dosage adjustment. May cause bleeding (due to thrombocytopenia) or infections (due to neutropenia), monitor closely. Patients must have platelet counts  $>100,000/\text{mm}^3$  and leukocytes  $>4000/\text{mm}^3$  for a repeat dose. Anemia may occur (less common and less severe than leukopenia or thrombocytopenia).

- Hepatic: Reversible increases in transaminases, bilirubin, and alkaline phosphatase have been reported (rare). Monitor liver function tests periodically during treatment.
- Infusion site reactions: Injection site burning and local tissue reactions, including swelling, pain, erythema, and necrosis have been reported. Monitor infusion site closely for infiltration or injection site reactions.

Pulmonary toxicity: Injection: **Dose-related pulmonary toxicity** (characterized by pulmonary infiltrates and/or fibrosis) **may occur; patients receiving cumulative doses  $>1400 \text{ mg/m}^2$  are at higher risk. Delayed onset of pulmonary fibrosis (may be fatal) has occurred in children up to 17 years after treatment**

## Dosage Forms:

Solution Reconstituted, Intravenous:

Bicnu: 100 mg (1 ea) [contains alcohol, usp]

Generic: 100 mg (1 ea)

Wafer, Implant:

Gliadel Wafer: 7.7 mg (8 ea) [contains polifeprosan 20]

Topical: requires compounding (10mg/100gm petrolatum)

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| Revision Date | Content Revised (Yes/No) | Contributors                               | Review/Revision Notes                                                                                                                               |
|---------------|--------------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| 1/24/17       | No                       | Catherine Sanders, MD; Robert Sterling, MD | Annual review                                                                                                                                       |
| 1/23/18       | No                       | Catherine Sanders, MD; Robert Sterling, MD | Annual review                                                                                                                                       |
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| 2/18/20       | No                       | Howard Taekman, MD; Robert Sterling, MD    | Annual review                                                                                                                                       |
| 8/3/21        | Yes                      | Howard Taekman, MD; Robert Sterling, MD    | Updated preauthorization criteria and Boxed Warnings section                                                                                        |
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| 2/13/24       | No                       | Howard Taekman, MD; Robert Sterling, MD    | Annual review                                                                                                                                       |
| 2/18/25       | Yes                      | Howard Taekman, MD; Robert Sterling, MD    | Added Off Label Use. Updated dosing information. Removed administration section and modified major adverse reactions and black box warning sections |