Lomustine: Drug information

(For additional information see "Lomustine: Patient drug information" and see "Lomustine: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Bone marrow suppression:

Lomustine causes myelosuppression, including fatal myelosuppression. Myelosuppression is delayed, dose-related, and cumulative, occurring 4 to 6 weeks after drug administration and persisting for 1 to 2 weeks. Thrombocytopenia is generally more severe than leukopenia. Cumulative myelosuppression from lomustine is manifested by greater severity and longer duration of cytopenias. Monitor blood counts for at least 6 weeks after each dose. Do not give lomustine more frequently than every 6 weeks.

Medication error prevention:

Prescribe, dispense, and administer only enough capsules for one dose. Fatal toxicity occurs with overdosage of lomustine. Both health care provider and pharmacist should emphasize to the patient that only one dose of lomustine is taken every 6 weeks.

Brand Names: US

Gleostine

Brand Names: Canada

CeeNU

Pharmacologic Category

Antineoplastic Agent, Alkylating Agent; Antineoplastic Agent, Alkylating Agent (Nitrosourea)

Dosing: Adult

Note: Dispense only enough capsules for a single dose; do not dispense more than one dose at a time (ISMP 2014). Repeat courses should only be administered after adequate recovery of leukocytes to >4,000/mm^3 and platelets to >100,000/mm^3. Doses should be rounded to the nearest 5 mg. Lomustine is associated with a moderate emetic potential; antiemetics are recommended to prevent nausea and vomiting.

Brain tumors: *Manufacturer's labeling:* Oral: 130 mg/m^2 as a single dose once every 6 weeks; reduce dose to 100 mg/m^2 as a single dose once every 6 weeks in patients with compromised bone marrow function (dosage reductions may be recommended for combination chemotherapy regimens).

Anaplastic oligodendroglioma: PCV regimen (off-label combination): Oral: 130 mg/m^2 on day 1

every 6 weeks for up to 4 cycles prior to radiation therapy (in combination with procarbazine and vincristine) (Cairncross 2013; Cairncross 2006).

Astrocytoma, high grade: POC regimen (off-label dosing): Adults ≤21 years: Oral: 100 mg/m^2 on day 1 every 6 weeks for 8 cycles (in combination with vincristine and prednisone) (Finlay 1995).

Glioblastoma, recurrent:

PCV regimen (off-label dosing): Oral: 110 mg/m^2 on day 1 every 6 weeks for 7 cycles (in combination with procarbazine and vincristine) (Levin 2000).

Single-agent therapy: Oral: 100 to 130 mg/m^2 every 6 weeks until disease progression or unacceptable toxicity (Wick 2010).

Medulloblastoma (off-label dosing): Adults ≤21 years: Oral: 75 mg/m^2 once every 6 weeks for 8 cycles (in combination with cisplatin and vincristine) (Packer 2006; Packer 1999).

Hodgkin lymphoma: *Manufacturer's labeling:* Oral: 130 mg/m^2 as a single dose once every 6 weeks; reduce dose to 100 mg/m^2 as a single dose once every 6 weeks in patients with compromised bone marrow function (dosage reductions may be recommended for combination chemotherapy regimens). **Note:** The use of lomustine in the management of Hodgkin lymphoma is limited due to efficacy of other chemotherapy agents/regimens.

Dosing: Pediatric

(For additional information see "Lomustine: Pediatric drug information")

Note: Dispense only enough capsules for a single dose; do not dispense more than one dose at a time (ISMP 2014). Repeat courses should only be administered after adequate recovery of leukocytes to >4,000/mm^3 and platelets to >100,000/mm^3. Doses should be rounded to the nearest 5 mg. Lomustine is associated with a moderate emetic potential; antiemetics are recommended to prevent nausea and vomiting (Dupuis 2011).

Brain tumors: *Manufacturer's labeling:* Oral: 130 mg/m^2 as a single dose once every 6 weeks; reduce dose to 100 mg/m^2 as a single dose once every 6 weeks in patients with compromised bone marrow function (dosage reductions may be recommended for combination chemotherapy regimens)

Astrocytoma, high grade: POC regimen (off-label dosing): Children ≥18 months and Adolescents: Oral: 100 mg/m^2 on day 1 every 6 weeks for 8 cycles (in combination with vincristine and prednisone) (Finlay 1995)

Medulloblastoma (off-label dosing): Children ≥3 years and Adolescents: Oral: 75 mg/m^2 once every 6 weeks for 8 cycles (in combination with cisplatin and vincristine) (Packer 2006; Packer 1999)

Hodgkin lymphoma: *Manufacturer's labeling:* Oral: 130 mg/m^2 as a single dose once every 6 weeks; reduce dose to 100 mg/m^2 as a single dose once every 6 weeks in patients with compromised bone marrow function (dosage reductions may be recommended for combination chemotherapy regimens). **Note:** The use of lomustine in the management of Hodgkin lymphoma is limited due to efficacy of other chemotherapy agents/regimens.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling. The following adjustments have been recommended:

Aronoff 2007: Adults:

CrCl 10 to 50 mL/minute: Reduce dose to 75% of normal dose

CrCl <10 mL/minute: Reduce dose to 25% to 50% of normal dose

Continuous ambulatory peritoneal dialysis (CAPD): Reduce dose to 25% to 50% of normal dose

Kintzel 1995:

CrCl 46 to 60 mL/minute: Reduce dose to 75% of normal dose

CrCl 31 to 45 mL/minute: Reduce dose to 70% of normal dose

CrCl ≤30 mL/minute: Avoid use

Hemodialysis: Due to its lipophilic nature, lomustine is not dialyzable (Canadian labeling). Supplemental dose is not necessary (Aronoff 2007).

Dosing: Hepatic Impairment There are no dosage adjustments provided in the manufacturer's labeling. However, lomustine is hepatically metabolized and caution should be used in patients with hepatic dysfunction.

Dosing: Obesity *ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer:* Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider 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: Dosing adjustment (based on nadir) for subsequent cycles:

Leukocytes ≥3,000/mm^3, platelets ≥75,000/mm^3: No dosage adjustment required

Leukocytes 2,000 to 2,999/mm^3, platelets 25,000 to 74,999/mm^3: Reduce dose to 70% of prior dose

Leukocytes <2,000/mm^3, platelets <25,000/mm^3: Reduce dose to 50% of prior dose

Nonhematologic toxicity: Pulmonary fibrosis: Discontinue permanently.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Capsule, Oral:

Gleostine: 5 mg, 10 mg, 40 mg, 100 mg

Generic: 10 mg [DSC], 40 mg [DSC], 100 mg [DSC]

Generic Equivalent Available (US) Yes

Dosage Forms: Canada Information with regard to form, strength, and availability of products uniquely available in Canada but currently not available in the US.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Capsule, Oral:

CeeNu: 10 mg, 40 mg, 100 mg

Administration

Lomustine is associated with a moderate emetic potential; antiemetics are recommended to prevent nausea and vomiting (Dupuis 2011).

Oral: Administering on an empty stomach may reduce the incidence of nausea and vomiting.

Varying strengths of capsules may be required to obtain necessary dose. Dispense only enough capsules for a single dose; do not dispense more than one dose at a time (ISMP 2014). Do not break capsules. If contact with skin occurs, immediately wash area (thoroughly). Avoid exposure to broken capsules.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. NIOSH recommends single gloving for administration of intact tablets or capsules (NIOSH 2016).

Use

Brain tumors: Treatment of primary and metastatic brain tumors (after appropriate surgical and/or radiotherapeutic procedures).

Hodgkin lymphoma: Treatment (in combination with other chemotherapy agents) of Hodgkin lymphoma which has progressed following initial chemotherapy; however, the use of lomustine in the management of Hodgkin lymphoma is limited due to efficacy of other chemotherapy agents/regimens.

Medication Safety Issues

Sound-alike/look-alike issues:

Lomustine may be confused with bendamustine, carmustine

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Administration issues:

Lomustine should only be administered as a single dose once every 6 weeks; serious and fatal adverse events have occurred when lomustine was inadvertently administered daily. The manufacturer and the Institute for Safe Medication Practices (ISMP) recommend prescribing, dispensing, and administering only enough capsules for a single dose (ISMP 2014).

Adverse Reactions

>10%:

Gastrointestinal: Nausea and vomiting, (onset: 3 to 6 hours after oral administration; duration: <24 hours)

Hematologic & oncologic: Leukopenia (65%; nadir: 5 to 6 weeks; recovery 6 to 8 weeks), bone marrow depression (dose-limiting, delayed, cumulative), thrombocytopenia (nadir: 4 weeks; recovery 5 to 6 weeks)

Frequency not defined:

Central nervous system: Ataxia, disorientation, dysarthria, lethargy

Dermatologic: Alopecia

Gastrointestinal: Stomatitis

Genitourinary: Azotemia (progressive), nephron atrophy, nephrotoxicity

Hematologic & oncologic: Acute leukemia, anemia, bone marrow dysplasia

Hepatic: Hepatotoxicity, increased serum alkaline phosphatase, increased serum bilirubin, increased serum transaminases

Ophthalmic: Blindness, optic atrophy, visual disturbance

Renal: Renal failure

Respiratory: Pulmonary fibrosis, pulmonary infiltrates

Contraindications

US labeling: There are no contraindications listed in the manufacturer's labeling.

Canadian labeling: Hypersensitivity to lomustine or any component of the formulation; severe leukopenia and/or thrombocytopenia.

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: **[US Boxed Warning]: Lomustine causes bone marrow suppression, including fatal myelosuppression. Hematologic toxicity is dose-related, cumulative, and delayed (occurring 4 to 6 weeks after drug administration and persisting for 1 to 2 weeks). Thrombocytopenia is generally more severe than leukopenia. Cumulative myelosuppression from lomustine is manifested by greater severity and longer duration of cytopenias. Monitor blood counts for at least 6 weeks after each dose. Do not administer lomustine more frequently than once every 6 weeks.** Dose adjustments should be based on nadir counts from prior dose. The Canadian labeling contraindicates use in patients with severe leukopenia and/or thrombocytopenia.

• Gastrointestinal toxicity: Lomustine is associated with a moderate emetic potential; antiemetics are recommended to prevent nausea and vomiting (Dupuis 2011). Stomatitis has also been reported.

• Hepatotoxicity: Hepatotoxicity (transaminase, alkaline phosphatase and bilirubin elevations) has been reported; monitor liver function.

• Pulmonary toxicity: May cause pulmonary toxicity (infiltrates and/or fibrosis). Pulmonary toxicity is usually related to cumulative doses >1,100 mg/m^2. May be delayed 6 months or longer after treatment initiation. Patients with baseline below 70% of predicted forced vital capacity or carbon monoxide diffusing capacity are at increased risk. Patients treated at a younger age may also be at increased risk for pulmonary toxicity. Monitor pulmonary function tests at baseline and frequently during treatment. Discontinue lomustine permanently in patients diagnosed with pulmonary fibrosis.

• Renal toxicity: Progressive renal failure with a decrease in kidney size has been reported. Use with caution in patients with renal impairment; may require dosage adjustment. Monitor renal function.

• Secondary malignancies: Long-term use of nitrosoureas is associated with the development of secondary malignancies, including acute leukemia and myelodysplasia.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special handling:

• Hazardous agent: Wear gloves when handling the bottle/capsules; if contact with skin occurs, immediately wash area (thoroughly).

Other warnings/precautions:

• Immunizations: Avoid immunization with live viral vaccines; may result in severe infection or lack of vaccine response.

• Medication error prevention: **[US Boxed Warning]: Lomustine should only be prescribed and dispensed as a single dose once every 6 weeks. Serious and fatal adverse events have occurred with overdosage (when lomustine was inadvertently administered daily). Health care providers, including pharmacists, should emphasize to the patient that only one dose of lomustine is taken every 6 weeks.** The Institute for Safe Medication Practices (ISMP) recommends that prescribers only prescribe one dose at a time and pharmacies dispense only

enough capsules for a single dose; in addition, patients should receive both verbal counseling and written instructions regarding proper dose and administration (ISMP 2014).

Metabolism/Transport Effects

Substrate of CYP2D6 (minor); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. Management: Avoid the use of lenograstim 24 hours before until 24 hours after the completion of myelosuppressive cytotoxic chemotherapy. *Risk D: Consider therapy modification*

Lipegfilgrastim: Antineoplastic Agents may diminish the therapeutic effect of Lipegfilgrastim. Management: Avoid concomitant use of lipegfilgrastim and myelosuppressive cytotoxic chemotherapy. Lipegfilgrastim should be administered at least 24 hours after the completion of myelosuppressive

cytotoxic chemotherapy. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk D: Consider therapy modification*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Pregnancy Implications Adverse effects have been observed in animal reproduction studies. Based on the mechanism of action, lomustine may cause fetal harm when administered to a pregnant

woman. Women of reproductive potential should use effective contraception during treatment and for 2 weeks after the final lomustine dose. Males with female partners of reproductive potential should use effective contraception during treatment and for 3.5 months (US labeling) or 6 months (Canadian labeling) after the final lomustine dose.

Breast-Feeding Considerations It is not known if lomustine is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, the manufacturer recommends that women not breast-feed during treatment and for 2 weeks after the final lomustine dose.

Monitoring Parameters CBC with differential and platelet count (weekly for at least 6 weeks after a dose), hepatic and renal function tests (periodic), pulmonary function tests (baseline and periodic)

Mechanism of Action Inhibits DNA, RNA, and protein synthesis via alkylation and carbamylation of DNA and RNA; lomustine is cell cycle non-specific (Perry 2012)

Pharmacodynamics/Kinetics

Distribution: Crosses blood-brain barrier; CNS concentrations are high (Perry 2012)

Metabolism: Hepatic to active metabolites (Perry 2012)

Half-life elimination: Metabolites: 16 to 48 hours

Time to peak, serum: ~3 hours (Perry 2012)

Excretion: Urine (~50%, as metabolites)

Pricing: US

Capsules (Gleostine Oral)

5 mg (5): $225.00

10 mg (5): $372.60

40 mg (5): $1490.40

100 mg (5): $4114.20

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

Brand Names: International Belustine (ES, FR, HN, IT, RU, TR); C.C.N.U. (ES); CCNU (AE, BH, CY, EG, GB, IL, IQ, IR, JO, KW, LB, LY, OM, PK, QA, SA, SY, TR, YE); Cecenu (BE, DE, GR, NL, PL); CEENU (AR, CN, MX, SG, UY); CeeNU (AU, BF, BJ, CI, CL, ET, GH, GM, GN, HK, KE, KR, LR, MA, ML, MR, MU, MW, NE, NG, NZ, PH, SC, SD, SL, SN, TN, TZ, UG, ZA, ZM, ZW); Ceenu (CZ); G-Lomustin (BD); Lomustine (IN, SE); Lomustine ”Medac” (DK); Lomustinum (PL); Lucostin (AT); Lucostine (FI); Prava (CH)