

LOMUSTINE
CAPSULES 10 mg,
40 mg, 100 mg

Rx only

LOMOOTHER 10, 40, 100

COMPOSITION:

LOMOOTHER 10

Each capsule contains:

Lomustine 10 mg
Excipients q.s.

Colour: approved colours used in capsule shell

LOMOOTHER 40

Each capsule contains:

Lomustine 40 mg
Excipients q.s.

Colour: approved colours used in capsule shell

LOMOOTHER 100

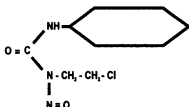
Each capsule contains:

Lomustine 100 mg
Excipients q.s.

Colour: approved colours used in capsule shell

DESCRIPTION:

Lomustine is an alkylating drug for oral administration. The chemical name for lomustine is 1-(2-chloro-ethyl)-3-cyclohexyl-1-nitrosourea and the molecular formula is $C_9H_{16}ClN_2O_2$. The molecular weight is 233.71. Lomustine is a yellow powder, which is soluble in 10% ethanol (0.05 mg per mL) and in absolute alcohol (70 mg per mL). Lomustine is insoluble in water (<0.05 mg per mL). The chemical structure is:



Lomustine Capsules is supplied as 10 mg, 40 mg, and 100 mg capsules and contains the following inactive ingredients: magnesium stearate and mannitol. The capsule shells are composed of gelatin and coloring pigments, depending on the strength: titanium dioxide, and/or yellow iron oxide, and/or Indigo line—FD&C Blue2.

INDICATIONS AND USAGE:

Brain Tumors

Lomustine Capsules is indicated for the treatment of patients with primary and metastatic brain tumors following appropriate surgical and/or radiotherapeutic procedures.

Hodgkin's Lymphoma

Lomustine Capsules is indicated as a component of combination chemotherapy for the treatment of patients with Hodgkin's lymphoma whose disease has progressed following initial chemotherapy.

DOSAGE AND ADMINISTRATION:

Important Prescribing and Dispensing Information

PRESCRIBE ONLY ONE DOSE FOR EACH TREATMENT CYCLE. DO NOT DISPENSE ENTIRE CONTAINER.

Dispense only a sufficient number of capsules for one dose. Confirm the total dose prescribed by the physician and the

appropriate combination of capsule strengths.

Dispense only the appropriate number of Lomustine Capsules required for the administration of a single dose.

The prescribed dose may consist of two or more different strengths and colors of capsules.

Instruct patients that Lomustine Capsules is taken as a single oral dose and will not be repeated for at least 6 weeks.

Taking more than the recommended dose causes toxicities, including fatal outcomes [see Warnings and Precautions and Overdosage]

Lomustine Capsules is a cytotoxic drug. Follow applicable special handling and disposal procedures.

To minimize the risk of dermal exposure, always wear impervious gloves when handling bottles containing Lomustine Capsules. Do not break Lomustine Capsules; avoid exposure to broken capsules. If dermal contact occurs, wash areas of skin contact immediately and thoroughly.

Recommended Dose

The recommended dose of Lomustine Capsules in adult and pediatric patients is 130 mg/m² taken as a single oral dose every 6 weeks. Round doses to the nearest 5 mg. Give as a single oral dose and do not repeat for at least 6 weeks. Reduce dose to 100 mg/m² every 6 weeks in patients with compromised bone marrow function. Also reduce dose accordingly when using with other myelosuppressive drugs.

Dose Modifications

Perform weekly complete blood counts and withhold each subsequent dose for more than 6 weeks if needed until platelet counts recover to 100,000/mm³ or greater and leukocytes recover to 4000/mm³ or greater [see Warnings and Precautions]

Modify each dose of Lomustine Capsules according to the hematologic response of the preceding dose as described in Table 1:

Table 1. Dose Modifications for Lomustine Capsules

Handle after Prior Dose		Dose Adjustment
Leukocytes (/mm ³)	Platelets (/mm ³)	
≥ 4000	≥ 100,000	None
3000 – 3999	75,000 – 99,999	None
2000 – 2999	25,000 – 74,999	Reduce dose by 30%
< 2000	< 25,000	Reduce dose by 50%

WARNINGS AND PRECAUTIONS:

Delayed Myelosuppression

Lomustine Capsules causes myelosuppression that can result in fatal infections and bleeding. Myelosuppression from Lomustine Capsules is delayed, dose-related, and cumulative. It usually occurs 4 to 6 weeks after drug administration and persists for 1 to 2 weeks. Thrombocytopenia is generally more severe than leukopenia. Cumulative myelosuppression from Lomustine Capsules 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 Capsules more frequently than every 6 weeks. Adjust dose based on nadir blood counts from prior dose [see Dosage and Administration]

Risk of Overdosage

Fatal toxicity occurs with over dosage of Lomustine Capsules. Dispensing or administering more than one dose can lead to fatal toxicity.

Prescribe only one dose at a time. Dispense only enough capsules for one dose. Both physician and pharmacist should emphasize to the patient that only one dose of Lomustine Capsules is taken every 6 weeks [see Dosage and Administration and Overdosage]

Pulmonary Toxicity

Pulmonary toxicity characterized by pulmonary infiltrates

Ther Dose

and/or fibrosis occurs with Lomustine Capsules. Patients with a baseline below 70% of the predicted Forced Vital Capacity (FVC) or Carbon Monoxide Diffusing Capacity (DLCO) are at increased risk. The onset of pulmonary toxicity occurs after an interval of 6 months or longer from the start of therapy, with cumulative doses of Lomustine Capsules usually greater than 1100 mg/m².

Obtain baseline pulmonary function tests prior to initiating treatment and repeat frequently during treatment. Permanently discontinue Lomustine Capsules in patients diagnosed with pulmonary fibrosis.

Secondary Malignancies

Secondary malignancies, including acute leukemia and myelodysplasia, occur with long term use.

Hepatotoxicity

Hepatic toxicity, manifested by increased levels of transaminases, alkaline phosphatase, and bilirubin occurs with Lomustine Capsules.

Monitor liver function.

Nephrotoxicity

Progressive renal failure with a decrease in kidney size occurs with Lomustine Capsules.

Monitor renal function.

Embryo-Fetal Toxicity

Based on animal data and its mechanism of action, Lomustine Capsules can cause fetal harm when administered to a pregnant woman. Embryo-fetal toxicity and teratogenicity occurred in rats and rabbits receiving lomustine daily during organogenesis at doses approximately two to four times the total human dose of 130 mg/m² over 6 weeks (0.18 to 0.27 times the single human dose of 130 mg/m²) based on body surface area (BSA). Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Lomustine Capsules and for 2 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Lomustine Capsules and for 3.5 months after the final dose.

CONTRAINDICATIONS:

None.

ADVERSE REACTIONS:

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Delayed myelosuppression [see Warnings and Precautions]
- Risks of overdosage [see Warnings and Precautions]
- Pulmonary toxicity [see Warnings and Precautions]
- Secondary malignancies [see Warnings and Precautions]
- Hepatotoxicity [see Warnings and Precautions]
- Nephrotoxicity [see Warnings and Precautions]

The following adverse reactions associated with the use of Lomustine Capsules were identified in clinical trials or postmarketing reports. Because these reactions were reported from a population of uncertain size, it is not possible to estimate their frequency, reliability, establishment a causal relationship to drug exposure.

Gastrointestinal disorders: nausea, vomiting, and stomatitis

Ocular disorders: optic atrophy, visual disturbances, and blindness

Neurologic disorders: disorientation, lethargy, ataxia, and dysarthria

Other: alopecia

OVERDOSAGE:

Overdosage with Lomustine Capsules has occurred, including fatal cases [see Dosage and Administration], Warnings and Precautions. Overdosage causes severe myelosuppression, as well as abdominal pain, diarrhea, vomiting, anorexia, lethargy, dizziness, abnormal hepatic function, cough, and shortness of breath.

No antidotes exist for Lomustine Capsules overdosage.

HOW SUPPLIED/STORAGE AND HANDLING:

How Supplied

Lomustine Capsules are available in four strengths and supplied as follows

LOMOOTHER 10 (Lomustine Capsules 10 mg) distinguishable by the color of the capsules, in individual bottle of 6 capsules each.

LOMOOTHER 40 (Lomustine Capsules 40 mg) distinguishable by the color of the capsules, in individual bottle of 6 capsules each.

LOMOOTHER 100 (Lomustine Capsules 100 mg) distinguishable by the color of the capsules, in individual bottle of 6 capsules each.

STORAGE AND HANDLING

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). Avoid temperatures over 40°C (104°F).

Lomustine Capsules is a cytotoxic drug. Follow applicable special handling and disposal procedures.

To minimize the risk of dermal exposure, always wear impervious gloves when handling bottles containing Lomustine Capsules. Do not break Lomustine Capsules; avoid exposure to broken capsules. If dermal contact occurs, wash areas of skin contact immediately and thoroughly.

REFERENCE LINK:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/017588s0431b1.pdf

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