

## Nitrosoureas

Nitrosoureas are a class of antineoplastic drugs. They require bioactivation by the liver and work as alkylating agents to cross-link DNA. They are able to cross the blood-brain barrier so are useful for brain tumors like glioblastoma. Notable side effects include myelosuppression, pulmonary fibrosis, and CNS toxicity. Examples of nitrosoureas include carmustine and lomustine.



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### Mechanism

#### Requires Bioactivation by Liver

##### Bioactivating Liver

Nitrosoureas require bioactivation by liver. This process involves hepatic cytochrome P450 enzymes.

#### Alkylating Agent

##### Elk-Agent

Alkylating agents are a class of antineoplastic drugs that transfer alkyl groups to DNA. This may result in the inhibition of protein synthesis that usually promotes cell growth. Alkylating agents are cell-cycle nonspecific.

#### Cross-links DNA

##### Linked DNA

When DNA is alkylated, alkyl group can form bonds between their hydrogen atoms. This cross-linking can occur between opposite strands, called interstrand, or within the same strand, called intrastrand. Cancer cells are most susceptible because of their high cell division rates.

#### Crosses Blood-Brain Barrier

##### BBB Wall

Nitrosoureas are lipophilic, which can cross the blood-brain barrier. Because of this ability, nitrosoureas are useful for treating CNS neoplasms.

### Indications

#### Glioblastoma

##### Glitter-blast Gladiator

These drugs are indicated for primary gliomas such as glioblastoma and other CNS neoplasms (e.g. brainstem glioma, medulloblastoma, ependymoma, and astrocytoma). Although they have been traditionally used for multiple myeloma and lymphomas, they are not commonly used now for these indications given their significant toxicity in comparison to other chemotherapeutic regimens.

### Side Effects

## Myelosuppression

### Suppressed Red and White Blood Cells

Because nitrosoureas affect all cells, normal cells characterized by rapid dividing cells such as hematopoietic, endothelial, and reproductive cells can be impacted. Bone marrow is the most sensitive tissue, resulting in bone marrow suppression (myelosuppression).

## Pulmonary Fibrosis

### Fiber-ball hitting Lungs

Pulmonary toxicity can occur and progress to irreversible pulmonary fibrosis. This adverse effect is dose-dependent. Patients may present with cough, dyspnea, reduced diffusion capacity, and a restrictive pulmonary function test pattern.

## CNS Toxicity

### CNS-brain with Toxic-green-glow

Signs and symptoms of central nervous system (CNS) toxicity include seizure, dizziness, and ataxia. Reversible hepatotoxicity is also seen in a small percentage of patients taking these medications.

## Drugs

### Carmustine

#### Car-mouse-tin

Carmustine is also known as BCNU (1,3-bis(2-chloroethyl)-1-nitrosourea). It forms intrastrand cross-links by binding to the N7 position of guanine. Carmustine can be given via intravenous injection to treat cerebral neoplasms, hodgkin and non-Hodgkin lymphomas, and multiple myeloma. Uniquely, carmustine can be used as an intracerebral implant (Gliadel wafer®) as adjunctive treatment of newly-diagnosed high-grade glioma or recurrent glioblastoma. Nausea and vomiting can develop 2 hours after administration and last in 4-6 hours.

### Lomustine

#### Love-mouse-tin

Lomustine is also known as CCNU (1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea). Lomustine is only administered orally, and it can be used for throat and larynx tumors, central nervous system tumors, lymphogranulomatosis, lung, and gastrointestinal tract cancer. Nausea and vomiting can develop 3-6 hours after administration.