BiCNU® (carmustine for injection)

DESCRIPTION

BiCNU® (carmustine for injection) is one of the nitrosoureas used in the treatment of certain neoplastic diseases. It is 1,3-bis(2-chloroethyl)-1-nitosourea. It is a yellow, powdery solid that is insoluble in water. BiCNU® is administered by intravenous infusion after reconstitution as recommended.

Sterile BiCNU is available in 100 mg single dose vials of lyophilized material.

PHARMACOLOGY

Although it is generally accepted that carmustine alkylates DNA and RNA, it is not cross resistant with other alkylators. As with other nitrosoureas, it may also inhibit several key enzymatic processes by carbamoylation of amino acids that are incorporated into proteins. Most such adverse reactions are reversible if detected early. When such effects or reactions do occur, the drug should be reduced in dosage or discontinued and appropriate corrective measures should be taken according to the clinical judgment of the physician. Reinstitution of BiCNU therapy should be considered.

PULMONARY TRAUMA: Pulmonary toxicity from BiCNU appears to be dose related. Patients receiving greater than 1400 mg/m² cumulative dose are at significantly higher risk than those receiving lower total doses.

DEFERRED PULMONARY TOXICITY: Occurs several years after treatment, and may result in death. Death occurs in some cases. In this long-term study, 8 of 17 patients (47%) who survived childhood brain tumors, including all the five patients initially treated at less than five years of age, died of pulmonary fibrosis.

Pulmonary fibrosis is a progressive condition causing increasing dyspnea and exercise intolerance. Efforts to save the patient's life may result in the administration of corticosteroids and other immunosuppressive drugs.

INDICATIONS AND USAGE

BiCNU® is indicated as palliative therapy as a single agent or in combination chemotherapy with other approved chemotherapeutic agents in the following:

2. Multiple myelomas—in combination with prednisone.
3. Hodgkin's Disease—in combination with other approved drugs in patients who relapse while being treated with primary therapy, or who fail to respond to primary therapy.
4. Non-Hodgkin's lymphomas—same as above.

CONTRAINDICATIONS

BiCNU® should not be given to individuals who have demonstrated a previous hypersensitivity to it.

WARNINGS

Since the major toxicity is delayed bone marrow suppression, blood counts should be monitored weekly for at least 6 weeks after a dose (see ADVERSE REACTIONS). At the recommended dosage, courses of BiCNU should not be given more frequently than every 6 weeks.

The bone marrow toxicity of BiCNU is cumulative and therefore dosage adjustments must be made to maintain a safe number of neutrophils or platelets (see Dosage Adjustment Table under DOSAGE AND ADMINISTRATION).

Pulmonary toxicity from BiCNU appears to be dose related. Patients receiving greater than 1400 mg/m² cumulative dose are at significantly higher risk than those receiving lower total doses. Additional delayed onset pulmonary fibrosis occurring up to 17 years after treatment has been reported in patients who received BiCNU in childhood and early adolescence (see ADVERSE REACTIONS).

Anemia also occurs, but is less frequent and less severe than thrombocytopenia. Hematologic Toxicity: A frequent and serious toxicity of BiCNU is delayed myelosuppression. It usually occurs 4 to 6 weeks after drug administration and is dose related. It is accompanied by a decrease in all four blood cell lines at about 4 weeks after treatment and persists for 1 to 2 weeks. Leukopenia occurs at 5 to 6 weeks after a dose of BiCNU and persists for 1 to 2 weeks. Thrombocytopenia generally occurs more severe than leukopenia. However, both may be dose limiting toxicities. BiCNU may produce cumulative myelosuppression, manifested by more progressive bone marrow depression as the cumulative dose of BiCNU increases. The occurrence of acute leukemia and bone marrow dysplasias have been reported in patients following long-term nitrosourea therapy.

Anemia also occurs, but is less frequent and less severe than thrombocytopenia.

Gastrointestinal Toxicity: Nausea and vomiting after I.V. administration of BiCNU are noted frequently. This toxicity appears within 2 hours of dosing, usually peaks within 15 minutes, and subsides by 2 hours. The severity of this effect is diminishing and sometimes preventing this side effect.

Hepatotoxicity: A reversible type of hepatic toxicity, manifested by icterus, elevation of hepatic enzymes above normal, and jaundice, has been reported in a small percentage of patients receiving BiCNU.

Nephrotoxicity: Renal ablation has been noted in a small percentage of patients receiving BiCNU. A repeat course of BiCNU (carmustine for injection) should not be given until blood marrow elements have returned to acceptable levels (platelets above 100,000/mm³, leukocytes above 4,000/mm³) and this is usually 6 weeks. Adequate neutrophil counts should be present on a peripheral blood smear. Blood counts should be monitored weekly and repeat courses delayed if counts fall below 100,000/mm³ and 4,000/mm³ within 6 weeks from the previous BiCNU administration.

Preparation of Intravenous Solutions: It is not advisable to use BiCNU® with any of the following drugs or solutions: erythropoietin, dexamethasone, thalidomide, methotrexate, or hypercortisol. BiCNU® should be used intravenously only and should be administered by I.V. drip injection of BiCNU® over shorter periods of time than 2 hours to produce intense pain and burning at the injection site of 1 mg BiCNU®.

Stability: Unopened vials of the drug must be stored in a refrigerator (2°C to 8°C, 36°F to 46°F). The recommended storage of unopened vials provides a stable product for 2 years. After reconstitution as recommended, BiCNU® is stable for 6 hours at room temperature (25°C, 77°F), protected from light.

Vials reconstituted as directed and further diluted to a concentration of 0.2 mg/mL in 50% Dextrose Injection, USP, should be stored at room temperature, protected from light and utilized within 8 hours.

Glass containers were used for the stability data provided in this section. Clear glass containers for BiCNU® administration.

HOW SUPPLIED

BiCNU® (carmustine for injection). Each package includes a vial containing 100 mg carmustine and a vial containing 3 mL sterile diluent.

DNC 0155-3012-38

Store dry powder in a refrigerator (2°C to 8°C, 36°F to 46°F). For information on package sizes available refer to the current price schedule.

REFERENCES


Manufactured by:

Ben Venue Laboratories, Inc., Bedford, Ohio 44146

BRISTOL LABORATORIES

ONCOLOGY PRODUCTS

A Bristol-Myers Squibb Company

Princeton, N.J. 08543 USA

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