250%

SPACE FOR BARCODE
Contains 25 mg Bendamustine HCl and 42.5 mg Mannitol USP. See insert for recommended dosage.

NDC 50912-109-13
Sterile **Rx Only**
Single-Use Vial

Bendamustine HCl For Injection

25 mg/vial

For Intravenous Infusion Only
Reconstitution and Dilution Required (see insert)

Reconstitute with 5 mL **Sterile Water for Injection, USP, to 5 mg/mL.** Immediately transfer to 0.9% Sodium Chloride Injection, USP, or 2.5% dextrose/0.45% Sodium Chloride Injection, USP (see insert)

Store up to 25°C (77°F) (See USP Controlled Room Temperature) **in original package.**

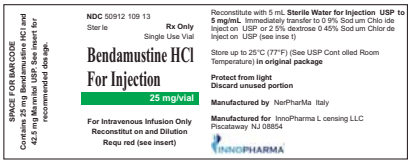
Protect from light.
Discard unused portion.

Manufactured by: NerPharMa, Italy

Manufactured for: InnoPharma Licensing LLC
Piscataway, NJ 08854

INNOPHARMA

Bendamustine Hydrochloride for Injection 25 mg/vial Vial Label
68 mm x 26 mm



250%

SPACE FOR BARCODE
Contains 100 mg Bendamustine HCl and 170 mg Mannitol USP. See insert for recommended dosage.

NDC 50912 110 17
Sterile **Rx Only**
Single Use Vial

Bendamustine HCl For Injection

100 mg/vial

For Intravenous Infusion Only
Reconstitution and Dilution Required (see insert)

Reconstitute with 20 mL **Sterile Water for Injection, USP, to 5 mg/mL.** Immediately transfer to 0.9% Sodium Chloride Injection, USP, or 2.5% dextrose/0.45% Sodium Chloride Injection, USP (see insert)

Store up to 25°C (77°F) (See USP Controlled Room Temperature) **in original package.**

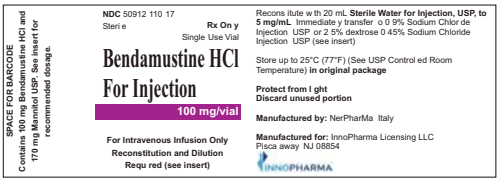
Protect from light.
Discard unused portion.

Manufactured by: NerPharMa, Italy

Manufactured for: InnoPharma Licensing LLC
Piscataway, NJ 08854

INNOPHARMA

Bendamustine Hydrochloride for Injection 100 mg/vial - Vial Label
83 mm x 29 mm



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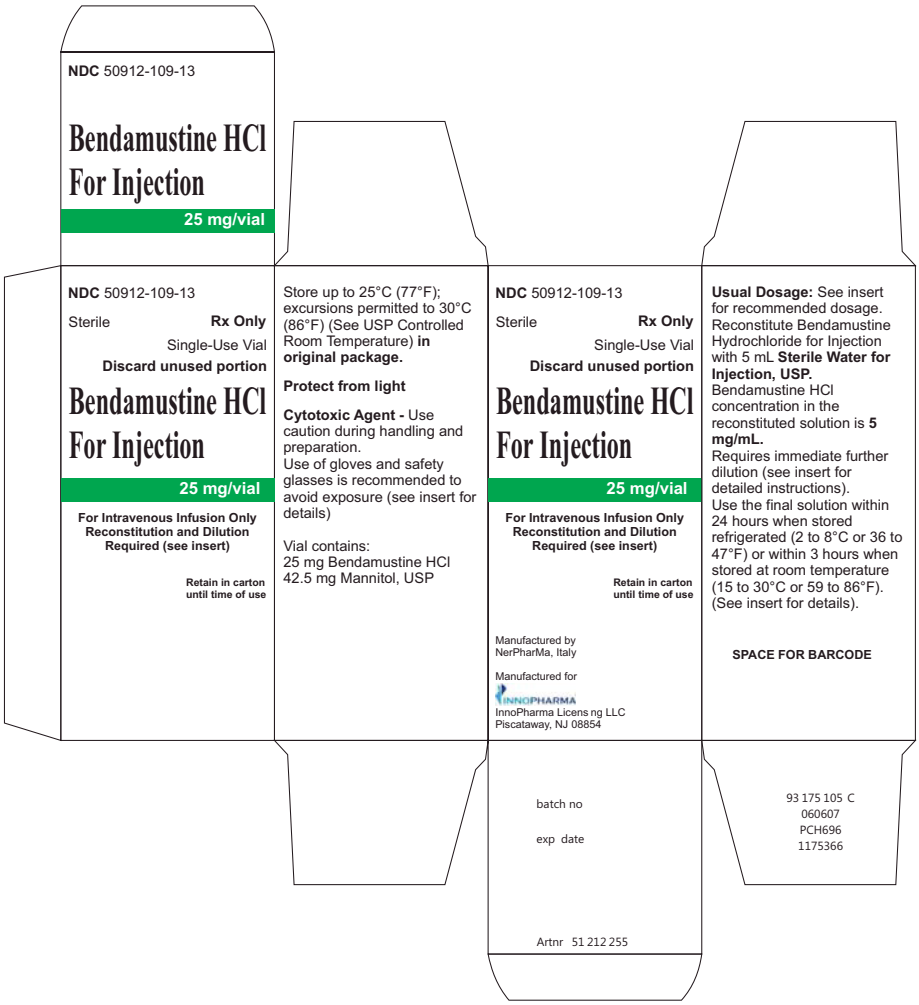
Developed on : 05/06/2015
Location : Nj 08854 USA
Dimension : LxWxH 36 x 36 x 80mm
Item-code : -
Barcode :
Packaging Component : 25mg/vial
Colours [redacted] (b) (4)
Style : Top Flap
Board :
Modified Date : 09/06/2015
Country : US
Revision No : 03
Path : D:Inno Pharma/ (b) (4)
Designed by : [redacted] (b) (4)



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Developed on : 05/06/2015
Location : Nj 08854 USA
Dimension : LxWxH 44 x 44 x 90mm
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Barcode :
Packaging Component : 100mg/vial
Colours : (b) (4)
Style : Top Flap
Board :
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Country : US
Revision No : 03
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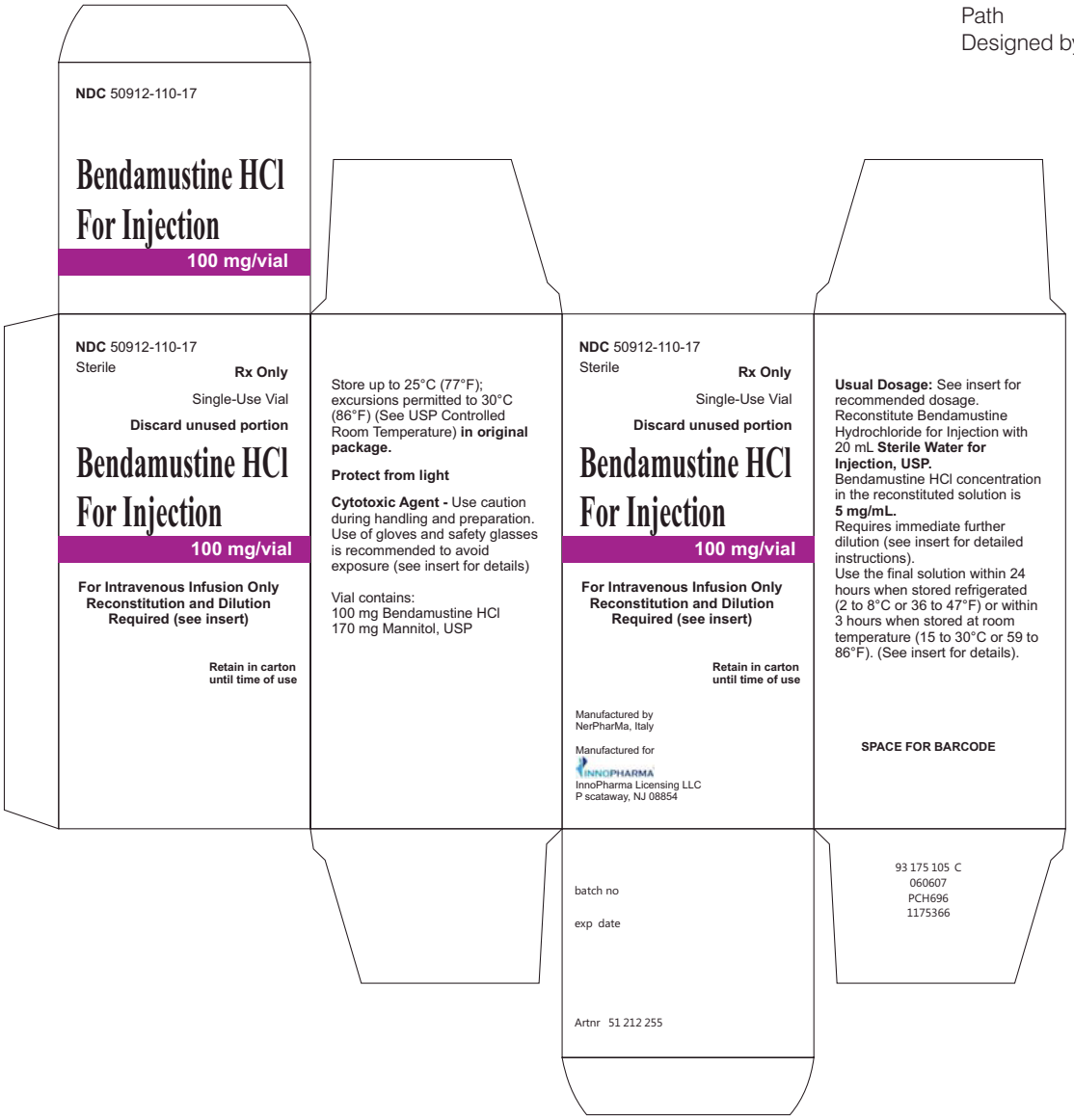
Designed by : (b) (4)



Front Page

Size:- 451 x 315 mm (3 ups) Font 6 pt

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BENDAMUSTINE HYDROCHLORIDE FOR INJECTION safely and effectively. See full prescribing information for BENDAMUSTINE HYDROCHLORIDE FOR INJECTION.

BENDAMUSTINE Hydrochloride for Injection, for intravenous use

Initial U.S. Approval: 2008

----------RECENT MAJOR CHANGES----------

Dosage and Administration (2)	09/2015
Selection of Bendamustine Hcl Formulation to Administer (2.1)	09/2015
Preparation for Intravenous Administration (2.4)	09/2015
Admixture Stability (2.5)	03/2015
Warnings and Precautions, Infections (5.2)	11/2015

----------INDICATIONS AND USAGE----------

Bendamustine Hydrochloride for Injection is an alkylating drug indicated for treatment of patients with:

- Chronic lymphocytic leukemia (CLL). Efficacy relative to first line therapies other than chlorambucil has not been established. (1.1)

----------DOSAGE AND ADMINISTRATION----------

Bendamustine Hydrochloride is available in two formulations, a solution (Bendamustine Hydrochloride Injection) and a lyophilized powder (Bendamustine Hydrochloride for Injection)(2.1)

For CLL:

- 100 mg/m^2 infused intravenously over 30 minutes on Days 1 and 2 of a 28 day cycle, up to 6 cycles (2.2)
- Dose modifications for hematologic toxicity: for Grade 3 or greater toxicity, reduce dose to 50 mg/m^2 on Days 1 and 2; if Grade 3 or greater toxicity recurs, reduce dose to 25 mg/m^2 on Days 1 and 2. (2.2)
- Dose modifications for non-hematologic toxicity: for clinically significant Grade 3 or greater toxicity, reduce the dose to 50 mg/m^2 on Days 1 and 2 of each cycle. (2.2)
- Dose re-escalation may be considered. (2.2)

General Dosing Considerations:

- Delay treatment for Grade 4 hematologic toxicity or clinically significant > Grade 2 non-hematologic toxicity. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

For Injection: 25 mg or 100 mg lyophilized powder in a single-dose vial for reconstitution. (3)

----------CONTRAINDICATIONS----------

Bendamustine Hydrochloride for Injection is contraindicated in patients with a history of a hypersensitivity reaction to bendamustine. Reactions have included anaphylaxis and anaphylactoid reactions. (5.3)

----------WARNING AND PRECAUTIONS----------

- Myelosuppression: Delay or reduce dose. Restart treatment based on ANC and platelet count recovery. (2.2) Complications of myelosuppression may lead to death. (5.1)
- Infections: Monitor for fever and other signs of infection or reactivation of infections and treat promptly. (5.2)
- Anaphylaxis and Infusion Reactions: Severe and anaphylactic reactions have occurred; monitor clinically and discontinue Bendamustine Hydrochloride for Injection. Premedicate in subsequent cycles for milder reactions. (5.3)
- Tumor Lysis Syndrome: Acute renal failure and death; anticipate and use supportive measures. (5.4)
- Skin Reactions: Discontinue for severe skin reactions. Cases of SJS and TEN, some fatal, have been reported when Bendamustine Hydrochloride for Injection was administered concomitantly with allopurinol and other medications known to cause these syndromes. (5.5)
- Other Malignancies: Pre-malignant and malignant diseases have been reported. (5.6)
- Extravasation Injury : Assure good venous access and monitor infusion site during and after administration. (5.7)
- Embryo-fetal toxicity: Fetal harm can occur when administered to a pregnant woman. Women should be advised to avoid becoming pregnant when receiving Bendamustine Hydrochloride for Injection. (5.8, 8.1)

----------ADVERSE REACTIONS----------

- Most common non-hematologic adverse reactions for CLL (frequency >15%) are pyrexia, nausea, and vomiting. (6.1)
- Most common hematologic abnormalities (frequency >15%) are lymphopenia, anemia, leukopenia, thrombocytopenia, and neutropenia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact InnoPharma Licensing LLC., at 1-732-885-2939 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------

Concomitant CYP1A2 inducers or inhibitors have the potential to affect the exposure of bendamustine. (7)

----------USE IN SPECIFIC POPULATIONS----------

- Renal Impairment : Do not use if CrCL is <40 mL/min. Use with caution in lesser degrees of renal impairment. (8.6)
- Hepatic Impairment : Do not use in moderate or severe hepatic impairment. Use with caution in mild hepatic impairment. (8.7)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 03/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Chronic Lymphocytic Leukemia (CLL)
Bendamustine Hydrochloride for Injection is indicated for the treatment of patients with chronic lymphocytic leukemia. Efficacy relative to first line therapies other than chlorambucil has not been established.

2 DOSAGE AND ADMINISTRATION

2.1 Selection of Bendamustine Hydrochloride Formulation to Administer
Bendamustine hydrochloride is available in two formulations, a solution (Bendamustine Hydrochloride Injection) and a lyophilized powder (Bendamustine Hydrochloride for Injection).

Bendamustine Hydrochloride Injection and the reconstituted Bendamustine Hydrochloride for Injection have different concentrations of bendamustine hydrochloride. The concentration of Bendamustine Hydrochloride insolution is 90 mg/mL and the concentration of bendamustine hydrochloride in the reconstituted solution of lyophilized powder is 5 mg/ml. **Do not mix or combine the two formulations.**

If a closed system transfer device (CSTD) or adaptor that contains polycarbonate or acrylonitrile-butadiene-styrene (ABS) is used as supplemental protection prior to dilution[1], only use Bendamustine Hydrochloride for Injection, the lyophilized powder formulation. [see *How Supplied/Storage and handling (16.1)*]

2.2 Dosing Instructions for CLL
Recommended Dosage:
The recommended dose is 100 mg/m^2 administered intravenously over 30 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles.

Dose Delays, Dose Modifications and Reinitiation of Therapy for CLL:
Bendamustine Hydrochloride for Injection administration should be delayed in the event of Grade 4 hematologic toxicity or clinically significant > Grade 2 non-hematologic toxicity. Once non-hematologic toxicity has recovered to < Grade 1 and/or the blood counts have improved [Absolute Neutrophil Count (ANC) > 1 x 10^9/L, platelets > 75 x 10^9/L], Bendamustine Hydrochloride for Injection can be reinitiated at the discretion of the treating physician. In addition, dose reduction may be warranted. *[see Warnings and Precautions (5.1)]*

Dose modifications for hematologic toxicity: for Grade 3 or greater toxicity, reduce the dose to 50 mg/m^2 on Days 1 and 2 of each cycle; if Grade 3 or greater toxicity recurs, reduce the dose to 25 mg/m^2 on Days 1 and 2 of each cycle.

Dose modifications for non-hematologic toxicity: for clinically significant Grade 3 or greater toxicity, reduce the dose to 50 mg/m^2 on Days 1 and 2 of each cycle. Dose re-escalation in subsequent cycles may be considered at the discretion of the treating physician.

2.4 Preparation for Intravenous Administration
Bendamustine Hydrochloride for Injection (25 mg/vial or 100 mg/vial Lyophilized powder)

If a closed system transfer device or adaptor that contains polycarbonate or ABS is to be used as supplemental protection during preparation[1], only use Bendamustine Hydrochloride for Injection, the lyophilized formulation.

- Each vial of Bendamustine Hydrochloride for Injection is intended for single dose only.
- Aseptically reconstitute each Bendamustine Hydrochloride for Injection vial as follows:
  - 25 mg Bendamustine Hydrochloride for Injection vial: Add 5 mL of only Sterile Water for Injection, USP.
  - 100 mg Bendamustine Hydrochloride for Injection vial: Add 20 mL of only Sterile Water for Injection, USP.
- Shake well to yield a clear, colorless to a pale yellow solution with a bendamustine HCl concentration of 5 mg/mL. The lyophilized powder should completely dissolve in 5 minutes. The reconstituted solution must be transferred to the infusion bag within 30 minutes of reconstitution. If particulate matter is observed, the reconstituted product should not be used.
- Aseptically withdraw the volume needed for the required dose (based on 5 mg/mL concentration) and immediately transfer to a 500 mL infusion bag of 0.9% Sodium Chloride Injection, USP (normal saline). As an alternative to 0.9% Sodium Chloride Injection, USP (normal saline), a 500 mL infusion bag of 2.5% Dextrose/0.45% Sodium Chloride Injection, USP, may be considered. The resulting final concentration of bendamustine HCl in the infusion bag should be within 0.2 to 0.6 mg/mL. After transferring, thoroughly mix the contents of the infusion bag.
- Visually inspect the filled syringe and the prepared infusion bag to ensure the lack of visible particulate matter prior to administration. The admixture should be a clear and colorless to slightly yellow solution.

Use Sterile Water for Injection, USP, for reconstitution and then either 0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP, for dilution, as outlined above. No other diluents have been shown to be compatible.

General Information
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Any unused solution should be discarded according to institutional procedures for antineoplastics.

2.5 Admixture Stability
Bendamustine Hydrochloride Injection and Bendamustine Hydrochloride for Injection contain no antimicrobial preservative. The admixture should be prepared as close as possible to the time of patient administration.

Bendamustine Hydrochloride for Injection (25 mg/vial or 100 mg/vial lyophilized powder)
Once diluted with either 0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP, the final admixture is stable for 24 hours when stored under refrigerated conditions at 2°to 8°C or (36° to 47°F) or for **3 hours** when stored at room temperature (15° to 30°C or 59° to 86°F) and room light. Administration of reconstituted and diluted Bendamustine Hydrochloride for Injection must be completed within this period.

3 DOSAGE FORMS AND STRENGTHS

- Bendamustine Hydrochloride for Injection: 25 mg or 100 mg white to off-white lyophilized powder in a single-dose vial for reconstitution

4 CONTRAINDICATIONS

Bendamustine Hydrochloride for Injection is contraindicated in patients with a known hypersensitivity (e.g., anaphylactic and anaphylactoid reactions) to bendamustine. *[see Warnings and Precautions (5.3)]*

5 WARNINGS AND PRECAUTIONS

5.1 Myelosuppression
Bendamustine hydrochloride for Injection caused severe myelosuppression (Grade 3-4) in 98% of patients in two studies for another indication. Three patients (2%) died from myelosuppression-related adverse reactions; one each from neutropenic sepsis, diffuse alveolar hemorrhage with Grade 3 thrombocytopenia, and pneumonia from an opportunistic infection (CMV).

In the event of treatment-related myelosuppression, monitor leukocytes, platelets, hemoglobin (Hgb), and neutrophils frequently. In the clinical trials, blood counts were monitored every week initially. Hematologic nadirs were observed predominantly in the third week of therapy. Myelosuppression may require dose delays or subsequent dose reductions if recovery to the recommended values has not occurred by the first day of the next scheduled cycle. Prior to the initiation of the next cycle of therapy, the ANC should be > 1 x 10^9/L and the platelet count should be >75 x 10^9/L. *[see Dosage and Administration (2.2)]*

5.2 Infections
Infection, including pneumonia,sepsis, septic shock, hepatitis and death have occurred in adult and pediatric patients in clinical trials and in postmarketing reports. Patients with myelosuppression following treatment with Bendamustine Hydrochloride for Injection are more susceptible to infections. Advise patients with myelosuppression following Bendamustine Hydrochloride for Injection treatment to contact a physician if they have symptoms or signs of infection.
Patients treated with Bendamustine Hydrochloride for Injection are at risk for reactivation of infections including (but not limited to) hepatitis B, cytomegalovirus, Mycobacterium tuberculosis, and herpes zoster. Patients should undergo appropriate measures (including clinical and laboratory monitoring, prophylaxis, and treatment) for infection and infection reactivation prior to administration.

5.3 Anaphylaxis and Infusion Reactions
Infusion reactions to Bendamustine Hydrochloride for Injection have occurred commonly in clinical trials. Symptoms include fever, chills, pruritus and rash. In rare instances severe anaphylactic and anaphylactoid reactions have occurred, particularly in the second and subsequent cycles of therapy. Monitor clinically and discontinue drug for severe reactions. Ask patients about symptoms suggestive of infusion reactions after their first cycle of therapy. Patients who experience Grade 3 or worse allergic-type reactions should not be rechallenged. Consider measures to prevent severe reactions, including antihistamines, antipyretics and corticosteroids in subsequent cycles in patients who have experienced Grade 1 or 2 infusion reactions. Discontinue Bendamustine Hydrochloride for Injection for patients with Grade 4 infusion reactions. Consider discontinuation for Grade 3 infusions reactions as clinically appropriate considering individual benefits, risks, and supportive care.

5.4 Tumor Lysis Syndrome
Tumor lysis syndrome associated with Bendamustine Hydrochloride for Injection treatment has occurred in patients in clinical trials and in postmarketing reports. The onset tends to be within the first treatment cycle of Bendamustine Hydrochloride for Injection and, without intervention, may lead to acute renal failure and death. Preventive measures include vigorous hydration and close monitoring of blood chemistry, particularly potassium and uric acid levels. Allopurinol has also been used during the beginning of Bendamustine Hydrochloride for Injection therapy. However, there may be an increased risk of severe skin toxicity when Bendamustine Hydrochloride for Injection and allopurinol are administered concomitantly *[see Warnings and Precautions (5.5)]*.

5.5 Skin Reactions
Skin reactions have been reported with Bendamustine Hydrochloride for Injection treatment in clinical trials and postmarketing safety reports including rash, toxic skin reactions and bullous exanthema. Some events occurred when Bendamustine Hydrochloride for Injection was given in combination with other anticancer agents.

In a study of Bendamustine Hydrochloride for Injection (90 mg/m^2) in combination with rituximab, one case of toxic epidermal necrolysis (TEN) occurred. TEN has been reported for rituximab (see rituximab package insert). Cases of Stevens-Johnson syndrome (SJS) and TEN, some fatal, have been reported when Bendamustine hydrochloride for Injection was administered concomitantly with allopurinol and other medications known to cause these syndromes. The relationship to Bendamustine Hydrochloride for Injection cannot be determined.

Where skin reactions occur, they may be progressive and increase in severity with further treatment. Monitor patients with skin reactions closely. If skin reactions are severe or progressive, withhold or discontinue Bendamustine Hydrochloride for Injection.

5.6 Other Malignancies
There are reports of pre-malignant and malignant diseases that have developed in patients who have been treated with Bendamustine Hydrochloride for Injection, including myelodysplastic syndrome, myeloproliferative disorders, acute myeloid leukemia and bronchial carcinoma. The association with Bendamustine Hydrochloride for Injection therapy has not been determined.

5.7 Extravasation Injury
Bendamustine Hydrochloride for Injection extravasations have been reported in postmarketing resulting in hospitalizations from erythema, marked swelling, and pain. Assure good venous access prior to starting Bendamustine Hydrochloride for Injection infusion and monitor the intravenous infusion site for redness, swelling, pain, infection, and necrosis during and after administration of Bendamustine Hydrochloride for Injection.

5.8 Embryo-fetal Toxicity
Bendamustine Hydrochloride for Injection can cause fetal harm when administered to a pregnant woman. Single intraperitoneal doses of bendamustine in mice and rats administered during organogenesis caused an increase in resorptions, skeletal and visceral malformations, and decreased fetal body weights. *[see Use in Specific Populations (8.1)]*

6 ADVERSE REACTIONS
The following serious adverse reactions have been associated with Bendamustine Hydrochloride in clinical trials and are discussed in greater detail in other sections of the label.

- Myelosuppression *[see Warnings and Precautions (5.1)]*
- Infections *[see Warnings and Precautions (5.2)]*
- Anaphylaxis and Infusion Reactions *[see Warnings and Precautions (5.3)]*
- Tumor Lysis Syndrome *[see Warnings and Precautions (5.4)]*
- Skin Reactions *[see Warnings and Precautions (5.5)]*
- Other Malignancies *[see Warnings and Precautions (5.6)]*
- Extravasation Injury *[see Warnings and Precautions (5.7)]*

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Chronic Lymphocytic Leukemia
The data described below reflect exposure to Bendamustine Hydrochloride for Injection in 153 patients with CLL studied in an active-controlled randomized trial. The population was 45 to 77 years of age, 63% male, 100% white, and were treatment naïve. All patients started the study at a dose of 100 mg/m^2 intravenously over 30 minutes on Days 1 and 2 every 28 days.

Adverse reactions were reported according to NCI CTC v.2.0. Non-hematologic adverse reactions (any grade) in the Bendamustine Hydrochloride for Injection group that occurred with a frequency greater than 15% were pyrexia (24%), nausea (20%), and vomiting (16%).

Other adverse reactions seen frequently in one or more studies included asthenia, fatigue, malaise, and weakness; dry mouth; somnolence; cough; constipation; headache; mucosal inflammation and stomatitis.

Worsening hypertension was reported in 4 patients treated with Bendamustine Hydrochloride for Injection in the CLL trial and in none treated with chlorambucil. Three of these 4 adverse reactions were described as a hypertensive crisis and were managed with oral medications and resolved.

The most frequent adverse reactions leading to study withdrawal for patients receiving Bendamustine Hydrochloride for Injection were hypersensitivity (2%) and pyrexia (1%).

Table 1 contains the treatment emergent adverse reactions, regardless of attribution, that were reported in ≥ 5% of patients in either treatment group in the randomized CLL clinical study.

Table 1: Non-Hematologic Adverse Reactions Occurring in Randomized CLL Clinical Study in at Least 5% of Patients

	Number (%) of patients			
	Bendamustine Hydrochloride for Injection (N=153)		Chlorambucil (N=143)	
System organ class Preferred term	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**
Total number of patients with at least 1 adverse reaction	121 (79)	52 (34)	96 (67)	25 (17)
Gastrointestinal Disorders				
Nausea	31 (20)	1 (<1)	21 (15)	1 (<1)
Vomiting	24 (16)	1 (<1)	9 (6)	0
Diarrhea	14 (9)	2 (1)	5 (3)	0
General disorders and administration site conditions				
Pyrexia	36 (24)	6 (4)	8 (6)	2 (1)
Fatigue	14 (9)	2 (1)	8 (6)	0
Asthenia	13 (8)	0	6 (4)	0
Chills	9 (6)	0	1 (<1)	0
Immune system disorders				
Hypersensitivity	7 (5)	2 (1)	3 (2)	0
Infections and infestations				
Nasopharyngitis	10 (7)	0	12 (8)	0
Infection	9 (6)	3 (2)	1 (<1)	1 (<1)
Herpes simplex	5 (3)	0	7 (5)	0
Investigations				
Weight decreased	11 (7)	0	5 (3)	0
Metabolism and nutrition disorders				
Hyperuricemia	11 (7)	3 (2)	2 (1)	0
Respiratory, thoracic and mediastinal disorders				
Cough	6 (4)	1 (<1)	7 (5)	1 (<1)
Skin and subcutaneous tissue disorders				
Rash	12 (8)	4(3)	7 (5)	3 (2)
Pruritus	8 (5)	0	2 (1)	0

The Grade 3 and 4 hematology laboratory test values by treatment group in the randomized CLL clinical study are described in Table 2. These findings confirm the myelosuppressive effects seen in patients treated with Bendamustine Hydrochloride. Red blood cell transfusions were administered to 20% of patients receiving Bendamustine Hydrochloride for Injection compared with 6% of patients receiving chlorambucil.

Table 2: Incidence of Hematology Laboratory Abnormalities in Patients Who Received Bendamustine Hydrochloride for Injection or Chlorambucil in the Randomized CLL Clinical Study

	Bendamustine Hydrochloride for Injection (N=150)		Chlorambucil (N=141)	
Laboratory Abnormality	**All Grades n %**	**Grade 3/4 n %**	**All Grades n %**	**Grade 3/4 n %**
Hemoglobin Decreased	134 (89)	20 (13)	115 (82)	12 (9)
Platelets Decreased	116 (77)	16 (11)	110 (78)	14 (10)
Leukocytes Decreased	92 (61)	42 (28)	26 (18)	4 (3)
Lymphocytes Decreased	102 (68)	70 (47)	27 (19)	6 (4)
Neutrophils Decreased	113 (75)	65 (43)	86 (61)	30 (21)

In the CLL trial, 34% of patients had bilirubin elevations, some without associated significant elevations in AST and ALT. Grade 3 or 4 increased bilirubin occurred in 3% of patients. Increases in AST and ALT of Grade 3 or 4 were limited to 1% and 3% of patients, respectively. Patients treated with Bendamustine Hydrochloride for Injection may also have changes in their creatinine levels. If abnormalities are detected, monitoring of these parameters should be continued to ensure that further deterioration does not occur.

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of Bendamustine Hydrochloride for Injection. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Blood and lymphatic systems disorders: Pancytopenia
Cardiovascular disorders: Atrial fibrillation, congestive heart failure (some fatal), myocardial infarction (some fatal), palpitation
General disorders and administration site conditions: Injection site reactions (including phlebitis, pruritus, irritation, pain, swelling), infusion site reactions (including phlebitis, pruritus, irritation, pain, swelling)
Immune system disorders: Anaphylaxis
Infections and infestations: Pneumocystis jiroveci pneumonia.
Respiratory, thoracic and mediastinal disorders: Pneumonitis
Skin and subcutaneous tissue disorders: Stevens-Johnson syndrome (with concomitant allopurinol and other medications known to cause the syndrome), Toxic

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epidermal necrolysis (with concomitant allopurinol and other medications known to cause the condition) *[see Warnings and Precautions (5.5)]*

7 DRUG INTERACTIONS
No formal clinical assessments of pharmacokinetic drug-drug interactions between Bendamustine Hydrochloride for Injection and other drugs have been conducted.
Bendamustine's active metabolites, gamma-hydroxy bendamustine (M3) and N-desmethyl-bendamustine(M4), are formed via cytochrome P450 CYP1A2. Inhibitors of CYP1A2 (e.g., fluvoxamine, ciprofloxacin) have potential to increase plasma concentrations of bendamustine and decrease plasma concentrations of active metabolites. Inducers of CYP1A2 (e.g., omeprazole, smoking) have potential to decrease plasma concentrations of bendamustine and increase plasma concentrations of its active metabolites. Caution should be used, or alternative treatments considered if concomitant treatment with CYP1A2 inhibitors or inducers is needed.

The role of active transport systems in bendamustine distribution has not been fully evaluated. *In vitro* data suggest that P-glycoprotein, breast cancer resistance protein (BCRP), and/or other efflux transporters may have a role in bendamustine transport.

Based on in *vitro data*, bendamustine is not likely to inhibit metabolism via human CYP isoenzymes CYP1A2, 2C9/10, 2D6, 2E1, or 3A4/5, or to induce metabolism of substrates of cytochrome P450 enzymes.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category D *[see Warnings and Precautions (5.8)]*

Risk Summary
Bendamustine Hydrochloride for Injection can cause fetal harm when administered to a pregnant woman. Bendamustine caused malformations in animals, when a single dose was administered to pregnant animals. Advise women to avoid becoming pregnant while receiving Bendamustine Hydrochloride for Injection and for 3 months after therapy has stopped. If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to a fetus. Advise men receiving Bendamustine Hydrochloride for Injection to use reliable contraception for the same time period.

Animal data
Single intraperitoneal doses of bendamustine from 210 mg/m^2 (70 mg/kg) in mice administered during organogenesis caused an increase in resorptions, skeletal and visceral malformations (exencephaly, cleft palates, accessory rib, and spinal deformities) and decreased fetal body weights. This dose did not appear to be maternally toxic and lower doses were not evaluated. Repeat intraperitoneal dosing in mice on gestation days 7 to 11 resulted in an increase in resorptions from 75 mg/m^2 (25 mg/kg) and an increase in abnormalities from 112.5 mg/m^2 (37.5 mg/kg) similar to those seen after a single intraperitoneal administration. Single intraperitoneal doses of bendamustine from 120 mg/m^2 (20 mg/kg) in rats administered on gestation days 4, 7, 9, 11, or 13 caused embryo and fetal lethality as indicated by increased resorptions and a decrease in live fetuses. A significant increase in external [effect on tail, head, and herniation of external organs (exomphalos)] and internal (hydronephrosis and hydrocephalus) malformations were seen in dosed rats. There are no adequate and well-controlled studies in pregnant women. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

8.3 Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants and tumorigenicity shown for bendamustine in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use
The effectiveness of Bendamustine Hydrochloride for Injection in pediatric patients has not been established. Bendamustine Hydrochloride for Injection was evaluated in a single Phase 1/2 trial in pediatric patients with leukemia. The safety profile for Bendamustine Hydrochloride for Injection in pediatric patients was consistent with that seen in adults, and no new safety signals were identified.

The trial included pediatric patients from 1 to 19 years of age with relapsed or refractory acute leukemia, including 27 patients with acute lymphocytic leukemia (ALL) and 16 patients with acute myeloid leukemia (AML). Bendamustine Hydrochloride for Injection was administered as an intravenous infusion over 60 minutes on Days 1 and 2 of each 21-day cycle. Doses of 90 and 120 mg/m^2 were evaluated. The Phase 1 portion of the study determined that the recommended Phase 2 dose of Bendamustine Hydrochloride for Injection in pediatric patients was 120 mg/m^2.

A total of 32 patients entered the Phase 2 portion of the study at the recommended dose and were evaluated for response. There was no treatment response (CR+ CRp) in any patient at this dose. However, there were 2 patients with ALL who achieved a CR at a dose of 90 mg/m^2 in the Phase 1 portion of the study.

In the above-mentioned pediatric trial, the pharmacokinetics of Bendamustine Hydrochloride for Injection at 90 and 120 mg/m^2 doses were evaluated in 5 and 38 patients, respectively, aged 1 to 19 years (median age of 10 years).

The geometric mean body surface adjusted clearance of bendamustine was 14.2 L/h/m^2. The exposures ($AUC_{0-\infty}$ and C_{max}) to bendamustine in pediatric patients following a 120 mg/m^2 intravenous infusion over 60 minutes were similar to those in adult patients following the same 120 mg/m^2 dose.

8.5 Geriatric Use
In CLL studies, there were no clinically significant differences in the adverse reaction profile between geriatric (≥65 years of age) and younger patients.

Chronic Lymphocytic Leukemia
In the randomized CLL clinical study, 153 patients received Bendamustine Hydrochloride for Injection. The overall response rate for patients younger than 65 years of age was 70% (n=82) for Bendamustine Hydrochloride for Injection and 30% (n=69) for chlorambucil. The overall response rate for patients 65 years or older was 47% (n=71) for Bendamustine Hydrochloride for Injection and 22% (n=79) for chlorambucil. In patients younger than 65 years of age, the median progression-free survival was 19 months in the Bendamustine Hydrochloride for Injection group and 8 months in the chlorambucil group. In patients 65 years or older, the median progression-free survival was 12 months in the Bendamustine Hydrochloride for Injection group and 8 months in the chlorambucil group.

8.6 Renal Impairment
No formal studies assessing the impact of renal impairment on the pharmacokinetics of bendamustine have been conducted. Bendamustine Hydrochloride for Injection should be used with caution in patients with mild or moderate renal impairment. Bendamustine Hydrochloride for Injection should not be used in patients with CrCL< 40 mL/min. *[see Clinical Pharmacology (12.3)]*

8.7 Hepatic Impairment
No formal studies assessing the impact of hepatic impairment on the pharmacokinetics of bendamustine have been conducted. Bendamustine Hydrochloride for Injection should be used with caution in patients with mild hepatic impairment. Bendamustine Hydrochloride for Injection should not be used in patients with moderate (AST or ALT 2.5 to 10 X ULN and total bilirubin 1.5 to 3 X ULN) or severe (total bilirubin > 3 X ULN) hepatic impairment. *[see Clinical Pharmacology (12.3)]*

8.8 Effect of Gender
No clinically significant differences between genders were seen in the overall incidences of adverse reactions in CLL study.

Chronic Lymphocytic Leukemia
In the randomized CLL clinical study, the overall response rate (ORR) for men (n=97) and women (n=56) in the Bendamustine Hydrochloride for Injection group was 60% and 57%, respectively. The ORR for men (n=90) and women (n=58) in the chlorambucil group was 24% and 28%, respectively. In this study, the median progression-free survival for men was 19 months in the Bendamustine Hydrochloride for Injection treatment group and 6 months in the chlorambucil treatment group. For women, the median progression-free survival was 13 months in the Bendamustine Hydrochloride for Injection treatment group and 8 months in the chlorambucil treatment group.

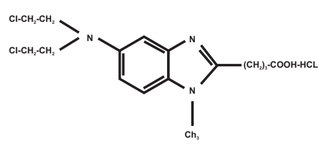
10 OVERDOSAGE

The intravenous LD_{50} of bendamustine HCl is 240 mg/m^2 in the mouse and rat. Toxicities included sedation, tremor, ataxia, convulsions and respiratory distress.

Across all clinical experience, the reported maximum single dose received was 280 mg/m^2. Three of four patients treated at this dose showed ECG changes considered dose-limiting at 7 and 21 days post-dosing. These changes included QT prolongation (one patient), sinus tachycardia (one patient), ST and T wave deviations (two patients) and left anterior fascicular block (one patient). Cardiac enzymes and ejection fractions remained normal in all patients.

No specific antidote for Bendamustine Hydrochloride for Injection overdose is known. Management of overdosage should include general supportive measures, including monitoring of hematologic parameters and ECGs.

11 DESCRIPTION
Bendamustine hydrochloride is an alkylating agent. The chemical name of bendamustine hydrochloride is 1H-benzimidazole-2-butanoic acid, 5-[bis(2-chloroethyl)amino]-1 methyl-, monohydrochloride. Its empirical molecular formula is $C_{16}H_{21}Cl_2N_3O_2 \cdot HCl$, and the molecular weight is 394.7. Bendamustine Hydrochloride contains a mechlorethamine group and a benzimidazole heterocyclic ring with a butyric acid substituent, and has the following structural formula:



Bendamustine Hydrochloride for Injection(25 mg/vial or 100 mg/vial lyophilized powder)
Bendamustine Hydrochloride for Injection is intended for intravenous infusion only after reconstitution with Sterile Water for Injection, USP, and after further dilution with either 0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP. It is supplied as a sterile non-pyrogenic white to off-white lyophilized powder in a single-dose vial. Each 25-mg vial contains 25 mg of bendamustine hydrochloride and 42.5 mg of mannitol, USP. Each 100-mg vial contains 100 mg of bendamustine hydrochloride and 170 mg of mannitol, USP. The pH of the reconstituted solution is 2.5 to 3.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Bendamustine is a bifunctional mechlorethamine derivative containing a purine-like benzimidazole ring. Mechlorethamine and its derivatives form electrophilic alkyl groups. These groups form covalent bonds with electron-rich nucleophilic moieties, resulting in interstrand DNA crosslinks. The bifunctional covalent linkage can lead to cell death via several pathways. Bendamustine is active against both quiescent and dividing cells. The exact mechanism of action of bendamustine remains unknown.

12.2 Pharmacodynamics
Based on the pharmacokinetics/pharmacodynamics analysis of data from adult NHL patients, nausea increased with increasing bendamustine C_{max}.

Cardiac Electrophysiology
The effect of bendamustine on the QTc interval was evaluated in 53 patients with indolent NHL and mantle cell lymphoma on Day 1 of Cycle 1 after administration of rituximab at 375 mg/m^2 intravenous infusion followed by a 30-minute intravenous infusion of bendamustine at 90 mg/m^2/day. No mean changes greater than 20 milliseconds were detected up to one hour post-infusion. The potential for delayed effects on the QT interval after one hour was not evaluated.

12.3 Pharmacokinetics
Absorption
Following a single IV dose of bendamustine hydrochloride C_{max} typically occurred at the end of infusion. The dose proportionality of bendamustine has not been studied.

Distribution
In vitro, the binding of bendamustine to human serum plasma proteins ranged from 94 to 96% and was concentration independent from 1 to 50 µg/mL. Data suggest that bendamustine is not likely to displace or to be displaced by highly protein-bound drugs. The blood to plasma concentration ratios in human blood ranged from 0.84 to 0.86 over a concentration range of 10 to 100 µg/mL indicating that bendamustine distributes freely in human red blood cells.

In a mass balance study, plasma radioactivity levels were sustained for a greater period of time than plasma concentrations of bendamustine, , hydroxybendamustine(M3), and N desmethylbendamustine(M4). This suggests that there are bendamustine derived materials (detected via the radiolabel), that are rapidly cleared and have a longer half-life than bendamustine and its active metabolites.

The mean steady-state volume of distribution (V_{ss}) of bendamustine was approximately 20 to 25 L. Steady-state volume of distribution for total radioactivity was approximately 50 L, indicating that neither bendamustine nor total radioactivity are extensively distributed into the tissues.

Metabolism
In vitro data indicate that bendamustine is primarily metabolized via hydrolysis to monohydroxy (HP1) and dihydroxy-bendamustine(HP2) metabolites with low cytotoxic activity. Two active minor metabolites, M3 and M4, are primarily formed via CYP1A2. However, concentrations of these metabolites in plasma are 1/10th and 1/100th that of the parent compound, respectively, suggesting that the cytotoxic activity is primarily due to bendamustine.

Results of a human mass balance study confirm that bendamustine is extensively metabolized via hydrolytic, oxidative, and conjugative pathways.

In vitro studies using human liver microsomes indicate that bendamustine does not inhibit CYP1A2, 2C9/10, 2D6, 2E1, or 3A4/5. Bendamustine did not induce metabolism of CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2E1, or CYP3A4/5 enzymes in primary cultures of human hepatocytes.

Elimination
Mean recovery of total radioactivity in cancer patients following IV infusion of [^{14}C] bendamustine hydrochloride was approximately 76% of the dose. Approximately 50 % of the dose was recovered in the urine and approximately 25 % of the dose was recovered in the feces. Urinary excretion was confirmed as a relatively minor pathway of elimination of bendamustine, with approximately 3.3% of the dose recovered in the urine as parent. Less than 1% of the dose was recovered in the urine as M3 and M4, and less than 5% of the dose was recovered in the urine as HP2.

Bendamustine clearance in humans is approximately 700 mL/minute. After a single dose of 120 mg/m^2 bendamustine IV over 1-hour the intermediate t½ of the parent compound is approximately 40 minutes. The mean apparent terminal elimination t½ of M3 and M4 are approximately 3 hours and 30 minutes respectively. Little or no accumulation in plasma is expected for bendamustine administered on Days 1 and 2 of a 28-day cycle.

Renal Impairment
In a population pharmacokinetic analysis of bendamustine in patients receiving 120 mg/m^2 there was no meaningful effect of renal impairment (CrCL 40 to 80 mL/min, N=31) on the pharmacokinetics of bendamustine. Bendamustine has not been studied in patients with CrCL< 40 mL/min.

These results are however limited, and therefore bendamustine should be used with caution in patients with mild or moderate renal impairment. Bendamustine should not be used in patients with CrCL< 40 mL/min. *[see Use in Specific Populations (8.6)]*

Hepatic Impairment
In a population pharmacokinetic analysis of bendamustine in patients receiving 120 mg/m^2 there was no meaningful effect of mild (total bilirubin ≤ ULN, AST ≥ ULN to 2.5 x ULN, and/or ALP ≥ ULN to 5.0 x ULN, N=26) hepatic impairment on the pharmacokinetics of bendamustine. Bendamustine has not been studied in patients with moderate or severe hepatic impairment.

These results are however limited, and therefore bendamustine should be used with caution in patients with mild hepatic impairment. Bendamustine should not be used in patients with moderate (AST or ALT 2.5 to 10 x ULN and total bilirubin 1.5 to 3 x ULN) or severe (total bilirubin > 3 x ULN) hepatic impairment. *[see Use in Specific Populations (8.7)]*

Effect of Age
Bendamustine exposure (as measured by AUC and C_{max}) has been studied in adult patients ages 31 through 84 years. The pharmacokinetics of bendamustine (AUC and C_{max}) were not significantly different between patients less than or greater than/equal to 65 years of age. *[see Use in Specific Populations (8.4, 8.5)]*

Effect of Gender
The pharmacokinetics of bendamustine were similar in male and female patients. *[see Use in Specific Populations (8.8)]*

Effect of Race
The effect of race on the safety, and/or efficacy of Bendamustine Hydrochloride for Injection has not been established. Based on a cross-study comparison, Japanese subjects (n = 6) had on average exposures that were 40% higher than non-Japanese subjects receiving the same dose. The significance of this difference on the safety and efficacy of Bendamustine Hydrochloride for Injection in Japanese subjects has not been established.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Bendamustine was carcinogenic in mice. After intraperitoneal Injections at 37.5 mg/m^2/day (12.5 mg/kg/day, the lowest dose tested) and 75 mg/m^2/day (25 mg/kg/day) for four days, peritoneal sarcomas in female AB/jena mice were produced. Oral administration at 187.5 mg/m^2/day (62.5 mg/kg/day, the only dose tested) for four days induced mammary carcinomas and pulmonary adenomas.

Bendamustine is a mutagen and clastogen. In a reverse bacterial mutation assay (Ames assay), bendamustine was shown to increase revertant frequency in the absence and presence of metabolic activation. Bendamustine was clastogenic in human lymphocytes *in vitro*, and in rat bone marrow cells *in vivo* (increase in micronucleated polychromatic erythrocytes) from 37.5 mg/m^2, the lowest dose tested.

Impaired spermatogenesis, azoospermia, and total germinal aplasia have been reported in male patients treated with alkylating agents, especially in combination with other drugs. In some instances spermatogenesis may return in patients in remission, but this may occur only several years after intensive chemotherapy has been discontinued. Patients should be warned of the potential risk to their reproductive capacities.

14 CLINICAL STUDIES

14.1 Chronic Lymphocytic Leukemia (CLL)
The safety and efficacy of Bendamustine Hydrochloride for Injection were evaluated in an open-label, randomized, controlled multicenter trial comparing Bendamustine Hydrochloride for Injection to chlorambucil. The trial was conducted in 301 previously-untreated patients with Binet Stage B or C (Rai Stages I - IV) CLL requiring treatment. Need-to-treat criteria included hematopoietic insufficiency, B-symptoms, rapidly progressive disease or risk of complications from bulky lymphadenopathy. Patients with autoimmune hemolytic anemia or autoimmune thrombocytopenia, Richter's syndrome, or transformation to prolymphocytic leukemia were excluded from the study.

The patient populations in the Bendamustine Hydrochloride for Injection and chlorambucil treatment groups were balanced with regard to the following baseline characteristics: age (median 63 vs. 66 years), gender (63% vs. 61% male), Binet stage (71% vs. 69% Binet B), lymphadenopathy (79% vs. 82%), enlarged spleen (76% vs. 80%), enlarged liver (48% vs. 46%), hypercellular bone marrow (79% vs. 73%), "B" symptoms (51% vs. 53%), lymphocyte count (mean 65.7x10^9/L vs. 65.1x10^9/L), and serum lactate dehydrogenase concentration (mean 370.2 vs. 388.4 U/L). Ninety percent of patients in both treatment groups had immunophenotypic confirmation of CLL (CD5, CD23 and either CD19 or CD20 or both).

Patients were randomly assigned to receive either Bendamustine Hydrochloride for Injection at 100 mg/m^2, administered intravenously over a period of 30 minutes on Days 1 and 2 or chlorambucil at 0.8 mg/kg (Broca's normal weight) administered orally on Days 1 and 15 of each 28-day cycle. Efficacy endpoints of objective response rate and progression-free survival were calculated using a pre-specified algorithm based on NCI working group criteria for CLL.

The results of this open-label randomized study demonstrated a higher rate of overall response and a longer progression-free survival for Bendamustine Hydrochloride for Injection compared to chlorambucil (see Table 5). Survival data are not mature.

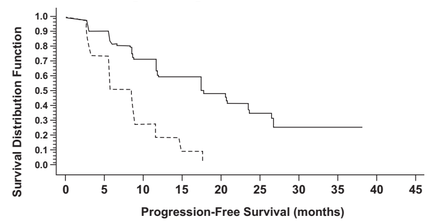
Table 5: Efficacy Data for CLL

	Bendamustine Hydrochloride for Injection (N=153)	Chlorambucil (N=148)	p-value
Response Rate n(%)			
Overall response rate	90 (59)	38 (26)	<0.0001
(95% CI)	(51.0, 66.6)	(18.6, 32.7)	
Complete response (CR)*	13 (8)	1 (<1)	
Nodular partial response (nPR)**	4 (3)	0	
Partial response (PR) †	73 (48)	37 (25)	
Progression-Free Survival††			
Median, months (95% CI)	18 (11.7, 23.5)	6 (5.6, 8.6)	
Hazard ratio (95% CI)	0.27 (0.17, 0.43)		<0.0001

CI = confidence interval
* CR was defined as peripheral lymphocyte count ≤4.0 x 10^9/L, neutrophils ≥1.5 x 10^9/L, platelets >100 x 10^9/L, hemoglobin > 110g/L, without transfusions, absence of palpable hepatosplenomegaly, lymph nodes ≤ 1.5 cm, < 30% lymphocytes without nodularity in at least a normocellular bone marrow and absence of "B" symptoms. The clinical and laboratory criteria were required to be maintained for a period of at least 56 days.
** nPR was defined as described for CR with the exception that the bone marrow biopsy shows persistent nodules.
† PR was defined as ≥ 50% decrease in peripheral lymphocyte count from the pretreatment baseline value, and either ≥50% reduction in lymphadenopathy, or ≥50% reduction in the size of spleen or liver, as well as one of the following hematologic improvements: neutrophils ≥ 1.5 x 10^9/L or 50% improvement over baseline, platelets >100 x 10^9/L or 50% improvement over baseline, hemoglobin >110g/L or 50% improvement over baseline without transfusions, for a period of at least 56 days.
†† PFS was defined as time from randomization to progression or death from any cause.

Kaplan-Meier estimates of progression-free survival comparing Bendamustine Hydrochloride for Injection with chlorambucil are shown in Figure 1.

Figure 1. Progression-Free Survival



Study Treatment Bendamustine Hydrochloride -----Chlorambucil

15 REFERENCES

1. OSHA Hazardous Drugs. OSHA. [Accessed on July 21, 2015, from http://www.osha.gov/SLTC/hazardousdrugs/index.html

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 Safe Handling and Disposal
Bendamustine Hydrochloride for Injection is a cytotoxic drug. Follow applicable special handling and disposal procedures.[1] Care should be exercised in the handling and preparation of solutions prepared from Bendamustine Hydrochloride for Injection. The use of gloves and safety glasses is recommended to avoid exposure in case of breakage of the vial or other accidental spillage. If gloves come in contact with Bendamustine Hydrochloride for Injection prior to dilution, remove gloves and follow disposal procedures[1]. If a solution of Bendamustine Hydrochloride for Injection contacts the skin, wash the skin immediately and thoroughly with soap and water. If Bendamustine Hydrochloride for Injection contacts the mucous membranes, flush thoroughly with water.

16.2 How Supplied
Bendamustine Hydrochloride for Injection is supplied in individual cartons as follows:

- NDC 50912-109-13: 25 mg white to off-white lyophilized powder in a 10 mL amber single-dose vial
- NDC 50912-110-17: 100 mg white to off-white lyophilized powder in a 30 mL amber single-dose vial

16.3 Storage
Bendamustine Hydrochloride for Injection(25 mg/vial or 100 mg/vial lyophilized powder).
Bendamustine Hydrochloride for Injection may be stored up to 25°C (77°F) with excursions permitted up to 30°C (86°F) (see USP Controlled Room Temperature). Retain in original package until time of use to protect from light.

17 PATIENT COUNSELING INFORMATION

Allergic (Hypersensitivity) Reactions
Inform patients of the possibility of mild or serious allergic reactions and to immediately report rash, facial swelling, or difficulty breathing during or soon after infusion.

Myelosuppression
Inform patients of the likelihood that Bendamustine Hydrochloride for Injection will cause a decrease in white blood cells, platelets, and red blood cells and the need for frequent monitoring of blood counts. Advise patients to report shortness of breath, significant fatigue, bleeding, fever, or other signs of infection.

Fatigue
Advise patients that Bendamustine Hydrochloride for Injection may cause tiredness and to avoid driving any vehicle or operating any dangerous tools or machinery if they experience this side effect.

Nausea and Vomiting
Advise patients that Bendamustine Hydrochloride for Injection may cause nausea and/or vomiting. Patients should report nausea and vomiting so that symptomatic treatment may be provided.

Diarrhea
Advise patients that Bendamustine Hydrochloride for Injection may cause diarrhea. Patients should report diarrhea to the physician so that symptomatic treatment may be provided.

Rash
Advise patients that a mild rash or itching may occur during treatment with Bendamustine Hydrochloride for Injection. Advise patients to immediately report severe or worsening rash or itching.

Pregnancy and Nursing
Bendamustine Hydrochloride for Injection can cause fetal harm. Women should be advised to avoid becoming pregnant throughout treatment and for 3 months after Bendamustine Hydrochloride for Injection therapy has stopped. Men receiving Bendamustine Hydrochloride for Injection should use reliable contraception for the same time period. Advise patients to report pregnancy immediately. Advise patients to avoid nursing while receiving Bendamustine Hydrochloride for Injection.

Manufactured by:
NerPharMa, Italy

Manufactured for:
InnoPharma Licensing LLC,
Piscataway, NJ 08854