alkylating agents or rituximab. However, the number of assessed patients is small.

Chronic lymphocytic leukemia
The indication for use in chronic lymphocytic leukemia is supported by a single open-label study comparing with chlorambucil. In the prospective, multicenter, randomized study, 319 previously untreated patients with chronic lymphocytic leukemia stage Binet B or C requiring therapy were included. The first line therapy with bendamustine hydrochloride 100 mg/m^2 i.v. on days 1 and 2 (BEN) was compared to treatment with chlorambucil 0.8 mg/kg days 1 and 15 (CLB) for 6 cycles in both arms. Patients received allopurinol in order to prevent tumor lysis syndrome.
Patients with BEN have a significantly longer median progression-free survival than patients with CLB treatment (21.5 versus 8.3 months, $p < 0.0001$ in the latest follow-up). Overall survival was not statistically significantly different (median not reached). The median duration of remission is 19 months with BEN and 6 months with CLB treatment ($p < 0.0001$). The safety evaluation in both treatment arms did not reveal any unexpected adverse reactions in nature and frequency. The dose of BEN was reduced in 34% of the patients. Treatment with BEN was discontinued in 3.9% of patients due to allergic reactions.

Indolent non-Hodgkin's lymphomas
The indication for indolent non-Hodgkin's lymphomas relied on two uncontrolled phase II trials.
In the pivotal, prospective, multi-center, open study 100 patients with indolent B-cell non- Hodgkin's lymphomas refractory to rituximab mono- or combination therapy were treated with BEN single agent. Patients received a median of 3 previous chemotherapy or biologic therapy courses. The median number of previous rituximab-containing courses was 2. The patients had no response or progress within 6 months after rituximab treatment. The dose of BEN was 120 mg/m^2 i.v. on days 1 and 2 planned for at least 6 cycles. Duration of treatment depended on response (6 cycles planned). The overall response rate was 75% including 17% complete (CR and CRu) and 58% partial response as assessed by independent review committee. The median duration of remission was 40 weeks. BEN was generally well tolerated when given in this dose and schedule.

The indication is further supported by another prospective, multicenter, open study including 77 patients. The patient population was more heterogeneous including: indolent or transformed B- cell non-Hodgkin's lymphomas refractory to rituximab mono- or combination therapy. The patients had no response or progress within 6 months or had an untoward reaction to prior rituximab treatment. Patients received a median of 3 previous chemotherapy or biological therapy courses. The median number of previous rituximab-containing courses was 2. The overall response rate was 76% with a median duration of response of 5 months (29 [95% CI 22.1, 43.1] weeks).

5.2 Pharmacokinetic properties
Distribution
The elimination half-life t1/2ß after 30 min i.v. infusion of 120 mg/m^2 area to 12 subjects was 28.2 minutes.
Following 30 min i.v. infusion the central volume of distribution was 19.3 L. Under steady- state conditions following i.v. bolus injection the volume of distribution was 15.8-20.5 L. More than 95% of the substance is bound to plasma proteins (primarily albumin).
Metabolism
A major route of clearance of is the hydrolysis to monohydroxy- and dihydroxy-. Formation of N-desmethyl- and gamma-hydroxy- by hepatic metabolism involves cytochrome P450 (CYP) 1A2 isoenzyme. Another major route of metabolism involves conjugation with glutathione.
In-vitro does not inhibit CYP 1A2, CYP 2C9/10, CYP 2D6, CYP 2E1 and CYP 3A4.
Elimination
The mean total clearance after 30 min i.v. infusion of 120 mg/m^2 body surface area to 12 subjects was 639.4 mL/minute. About 20% of the administered dose was recovered in urine within 24 hours. Amounts excreted in urine were in the order monohydroxy- > > dihydroxy- > oxidized metabolite > N-desmethyl. In the bile, primarily polar metabolites are eliminated.
Hepatic impairment
In patients with 30 - 70% tumor infestation of the liver and mild hepatic impairment (serum bilirubin < 1.2 mg/dL) the pharmacokinetic behavior was not changed. There was no significant difference to patients with normal liver and kidney function with respect to C_{max}, t^{max}, AUC, t1/2ß, volume of distribution and clearance. AUC and total body clearance of correlate inversely with serum bilirubin.
Renal impairment
In patients with creatinine clearance > 10 mL/min including dialysis dependent patients, no significant difference to patients with normal liver and kidney function was observed with respect to Cmax, tmax, AUC, t1/2ß, volume of distribution and clearance.
Elderly subjects
Subjects up to 84 years of age were included in pharmacokinetic studies. Higher age does not influence the pharmacokinetics of bendamustine hydrochloride.

Non-Clinical Information
Bendamustine hydrochloride induces aberrations of the chromosomes and is mutagenic in-vivo as well as in-vitro. In long-term studies in female mice bendamustine hydrochloride is carcinogenic.

5.3 Preclinical safety data
Not Applicable

6. Pharmaceutical Particulars
6.1 List of excipients
Mannitol

6.2 Incompatibilities
This medicinal product should not be mixed with other medicinal products except those mentioned in Instructions for Use and Handling and Disposal.

6.3 Shelf life
Unopened vial:
24 months
Keep the vial in the outer carton in order to protect from light. Store below 30 °C in original packaging.

After reconstitution/dilution:
The powder should be reconstituted immediately after opening of the vial.
The reconstituted concentrate should be diluted immediately with 0.9% sodium chloride solution.

Solution for Infusion:
After reconstitution and dilution, chemical and physical stability has been demonstrated for 3.5 hours at 25 ºC/ 60%RH and 2 days at 2 °C to 8 °C in polyethylene bags.
From a microbiological point of view, the solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage
Unopened vial:
The powder should be reconstituted immediately after opening of the vial.
The reconstituted concentrate should be diluted immediately with 0.9% sodium chloride solution.

Solution for Infusion
After reconstitution and dilution, chemical and physical stability has been demonstrated for 3.5 hours at 25 ºC/ 60%RH and 2 days at 2 °C to 8 °C in polyethylene bags.
From a microbiological point of view, the solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Storage Conditions
Keep the vial in the outer carton in order to protect from light. Store below 30 °C in original packaging.
For storage conditions of the reconstituted or diluted medicinal product, see Shelf life

6.5 Nature and contents of container
Bendamustine hydrochloride Powder for Concentrate for Solution for Infusion 100 mg/vial is filled in 50 ml glass vial type I with reinforced Non-PVC Base, closed with 20 mm grey butyl slotted rubber plug and 20 mm colored flip off seal and packed in to carton along with pack insert.

6.6 Instructions for Use and Handling
When handling bendamustine hydrochloride, inhalation, skin contact or contact with mucous membranes should be avoided (wear gloves and protective clothes!). Contaminated body parts should be carefully rinsed with water and soap, the eye should be rinsed with physiological saline solution. If possible, it is recommended to work on special safety workbenches (laminar flow) with liquid impermeable, absorbing disposable foil. Pregnant personnel should be excluded from handling cytostatics.
The powder for concentration for solution for infusion has to be reconstituted with water for injection, diluted with sodium chloride 9 mg/mL (0.9%) solution for injection and then administered by intravenous infusion. Aseptic technique is to be used.
1. Reconstitution
Reconstitute each vial of bendamustine hydrochloride containing 100 mg bendamustine hydrochloride in 40 mL water for injection by shaking.
The reconstituted concentrate contains 2.5 mg bendamustine hydrochloride per mL and appears as a clear colorless solution.
2. Dilution
As soon as a clear solution is obtained (usually after 5-10 minutes), dilute the total recommended dose of bendamustine hydrochloride immediately with 0.9% NaCl solution to produce a final volume of about 500 mL.
Bendamustine hydrochloride must be diluted with 0.9% NaCl solution and not with any other injectable solution.
3. Administration
The solution is administered by intravenous infusion over 30-60 min.
The vials are for single use only.

7. Manufactured by
VENUS REMEDIES LIMITED
Hill Top Industrial Estate, Jharmajri, EPIP Phase I Extension
Bhatoli Kalan, Solan, Baddi, 173205, India

8. Product Registration Holder
Unimed SDN. Bhd.
No. 53, Jalan Tembaga SD 5/2B,
Bandar Sri Damansara, 52200,
Kuala Lumpur, Malaysia

9. Date of Revision
November 2025

℞

VENUS®
Enjoy Innovations

1. Name of the Medicinal Product
Bendamustine Hydrochloride 100mg Powder for Concentrate for Solution for Infusion

2. Qualitative and Quantitative Composition
Each vial contains:
Bendamustine Hydrochloride…… 100 mg
(as Bendamustine Hydrochloride Monohydrate)

3. Pharmaceutical Form
Powder for Concentrate for Solution for Infusion

4. Clinical Particulars
4.1 Therapeutic indications
Bendamustine hydrochloride is indicated for monotherapy in patients with chronic lymphocytic leukaemia. Efficacy relative to first line therapies other than chlorambucil has not been established.
Bendamustine hydrochloride is indicated for monotherapy in patients with indolent B-cell non-Hodgkin's lymphomas that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

4.2 Posology and method of administration
Posology
For intravenous infusion over 30 - 60 minutes. (See Special precautions for disposal and other handling).
Infusion must be administered under the supervision of a physician qualified and experienced in the use of chemotherapeutic agents.
Poor bone marrow function is related to increased chemotherapy-induced haematological toxicity. Treatment should not be started if leukocyte and/or platelet values have dropped to < 3,000/µl or < 75,000/µl, respectively (see Contraindications).
Monotherapy for chronic lymphocytic leukaemia
100 mg/m^2 body surface area bendamustine hydrochloride on days 1 and 2; every 4 weeks.
Monotherapy for indolent non-Hodgkin's lymphomas refractory to rituximab
120 mg/m^2 body surface area bendamustine hydrochloride on days 1 and 2; every 3 weeks.

Treatment should be terminated or delayed if leukocyte and/or platelet values drop to < 3000/µL or < 75000/µL, respectively. Treatment can be continued after leukocyte values have increased to > 4000/µL and platelet values to > 100000/µL.
The leukocyte and platelet nadir is reached after 14-20 days with regeneration after 3-5 weeks. During therapy free intervals strict monitoring of the blood count is recommended (see Warnings and Precautions).
In case of non-hematological toxicity, dose reductions have to be based on the worst common toxicity criteria (CTC) grades in the preceding cycle. A 50% dose reduction is recommended in case of CTC grade 3 toxicity.
An interruption of treatment is recommended in case of CTC grade 4 toxicity.
If a patient requires a dose modification, the individually calculated reduced dose must be given on day 1 and 2 of the respective treatment cycle.
For preparation and administration instructions, see Instructions for Use and Handling.

Hepatic impairment
On the basis of pharmacokinetic data, no dose adjustment is necessary in patients with mild hepatic impairment (serum bilirubin < 1.2 mg/dL). A 30% dose reduction is recommended in patients with moderate hepatic impairment (serum bilirubin 1.2 - 3.0 mg/dL).
No data are available in patients with severe hepatic impairment (serum bilirubin values of > 3.0 mg/dL) (see Contraindications).

Renal impairment
On the basis of pharmacokinetic data, no dose adjustment is necessary in patients with a creatinine clearance of > 10 mL/min. Experience in patients with severe renal impairment is limited.

Pediatric patients
As there are limited data, the safety and efficacy of in pediatric patients has not been established.

Elderly patients
There is no evidence that dose adjustments are necessary in elderly patients (see Pharmacokinetic Properties).
Route of Administration:
For intravenous infusion over 30 - 60 minutes. (See Instructions for Use and Handling and Disposal).

4.3 Contraindications
- Hypersensitivity to the active substance or to any of the excipients (see List of Excipients)
- During breast-feeding
- Severe hepatic impairment (serum bilirubin > 3.0 mg/dL)
- Jaundice
- Severe bone marrow suppression and severe blood count alterations (leukocyte and/or platelet values dropped to < 3000/µL or < 75000/µL, respectively)
- Major surgery less than 30 days before start of treatment
- Infections, especially involving leukocytopenia
- Yellow fever vaccination

4.4 Special warnings and precautions for use
Myelosuppression
Patients treated with bendamustine hydrochloride may experience myelosuppression (bone marrow failure). In the event of treatment-related myelosuppression, leukocytes, platelets, hemoglobin, and neutrophils

should be monitored and re-evaluated prior to initiation of the next cycle of therapy. Prior to the initiation of the next cycle of therapy, the following parameters are recommended: Leukocyte and/or platelet values > 4000/µL or > 100000/µL, respectively. Treatment-related myelosuppression may require dose adjustment and/or dose delays.
Treatment with bendamustine hydrochloride may cause prolonged lymphocytopenia (< 600/µL) and low CD4-positive T-cell (T-helper cell) counts (< 200/µL) for at least 7–9 months after the completion of treatment. Lymphocytopenia and CD4-positive T-cell depletion are more pronounced when is combined with rituximab. Patients with lymphopenia and low CD4-positive T-cell count following treatment with bendamustine hydrochloride are more susceptible to (opportunistic) infections.
Bendamustine hydrochloride should not be used during severe bone marrow suppression and severe blood count alterations. See *Dosage and Administration.*
Infections
Serious and fatal infections, including fatal sepsis, have occurred with treatment. These infections included bacterial (pneumonia) and opportunistic infections such as Pneumocystis Jirovecii Pneumonia (PJP), Varicella Zoster Virus (VZV) and Cytomegalovirus (CMV). Cases of progressive multifocal leukoencephalopathy (PML) including fatal ones have been reported following the use of mainly in combination with rituximab or obinutuzumab. Patients with lymphopenia and low CD4-positive T-cell count following treatment with bendamustine hydrochloride are more susceptible to (opportunistic) infections. In case of low CD4-positive T-cell counts (< 200/µL) Pneumocystis jirovecii pneumonia (PJP) prophylaxis should be considered. All patients should be monitored for respiratory signs and symptoms throughout treatment. Discontinuation of bendamustine hydrochloride should be considered if there are signs of (opportunistic) infections. Consider PML in the differential diagnosis in patients with new or worsening neurological, cognitive or behavioural signs or symptoms. If PML is suspected then appropriate evaluations should be undertaken and treatment suspended until PML is excluded.
Skin reactions
A number of skin reactions have been reported. These events have included rash, toxic skin reactions and bullous exanthema. Cases of Stevens – Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), some fatal, have also been reported. Some events of SJS and TEN occurred when bendamustine hydrochloride was administered concomitantly with allopurinol or when bendamustine hydrochloride was given in combination with other anticancer agents. Cases of drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with the use of bendamustine hydrochloride in combination with rituximab. Where skin reactions occur, they may be progressive and increase in severity with further treatment; therefore, patients with skin reactions should be monitored closely. If skin reactions are severe or progressive, bendamustine hydrochloride should be withheld or discontinued. For severe skin reactions where a relationship to bendamustine hydrochloride is suspected, treatment should be discontinued.
Patients with cardiac disorders
During treatment with bendamustine hydrochloride, the concentration of potassium in the blood should be closely monitored. Potassium supplementation should be given when K+ < 3.5 mEq/L, and ECG measurement must be performed.
Fatal cases of myocardial infarction and cardiac failure have been reported with treatment. Patients with concurrent or history of cardiac disease should be observed closely.
Nausea, vomiting
An antiemetic may be given for the symptomatic treatment of nausea and vomiting.
Tumor lysis syndrome
Tumor lysis syndrome associated with bendamustine hydrochloride treatment has been reported in patients in clinical trials. The onset tends to be within 48 hours of the first dose of bendamustine hydrochloride and, without intervention, may lead to acute renal failure and death. Preventive measures include adequate
volume status, close monitoring of blood chemistry, particularly potassium and uric acid levels. The use of allopurinol during the first one to two weeks of bendamustine hydrochloride therapy can be considered but not necessarily as standard.
Anaphylaxis
Infusion reactions to bendamustine hydrochloride have occurred commonly in clinical trials. Symptoms are generally mild and include fever, chills, pruritus and rash. In rare instances severe
anaphylactic and anaphylactoid reactions have occurred. Patients must be asked about symptoms suggestive of infusion reactions after their first cycle of therapy. Measures to prevent severe reactions, including administration of antihistamines, antipyretics and corticosteroids must be considered in subsequent cycles in patients who have previously experienced infusion reactions.
Patients who experienced Grade 3 or worse allergic-type reactions were typically not re- challenged.
Contraception
Bendamustine hydrochloride is teratogenic and mutagenic.
Women should not become pregnant during treatment. Male patients should not father a child during and up to 6 months after treatment. They should seek advice about sperm conservation prior to treatment with bendamustine hydrochloride because of possible irreversible infertility.
Extravasation
An extravasal injection should be stopped immediately. The needle should be removed after a short aspiration. Thereafter, the affected area of tissue should be cooled. The arm should be elevated. Additional treatments, such as the use of corticosteroids, are not of clear benefit.
Non-melanoma skin cancer
In clinical studies, an increased risk for non-melanoma skin cancers (basal cell carcinoma and squamous cell carcinoma) has been observed in patients treated with containing therapies. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.
Other malignancies
There are reports of secondary tumors, including myelodysplastic syndrome, myeloproliferative disorders, acute myeloid leukemia and bronchial carcinoma. The association with therapy has not been determined.
Hepatitis B reactivation
Reactivation of hepatitis B in patients who are chronic carriers of this virus has occurred after these patients received bendamustine hydrochloride. Some cases resulted in acute hepatic failure or a fatal outcome. Patients should be tested for HBV infection before initiating treatment with bendamustine hydrochloride. Carriers of HBV who require treatment with bendamustine hydrochloride should be closely monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy. See Adverse Reactions.

4.5 Interaction with other medicinal products and other forms of interaction
No in-vivo interaction studies have been performed.
When bendamustine hydrochloride is combined with myelosuppressive agents, the effect of bendamustine

hydrochloride and/or the co-administered medicinal products on the bone marrow may be potentiated. Any treatment reducing the patient's performance status or impairing bone marrow function can increase the toxicity of bendamustine hydrochloride.
Combination of bendamustine hydrochloride with cyclosporine or tacrolimus may result in excessive immunosuppression with risk of lymphoproliferation.
Cytostatics can reduce antibody formation following live-virus vaccination and increase the risk of infection, which may lead to fatal outcome. This risk is increased in subjects who are already immunosuppressed by their underlying disease.
Metabolism involves cytochrome P450 (CYP) 1A2 isoenzyme (see Pharmacokinetic Properties). Therefore, potential for interaction with CYP1A2 inhibitors (such as fluvoxamine, ciprofloxacin, acyclovir, cimetidine) exists.

4.6 Fertility, pregnancy and lactation
Pregnancy
There are insufficient data from the use of bendamustine hydrochloride in pregnant women. In non-clinical studies was embryo-/fetolethal, teratogenic and genotoxic (see Non-Clinical Information). Women of childbearing potential must use effective methods of contraception both before, during, and one month following bendamustine hydrochloride therapy.
During pregnancy, bendamustine hydrochloride should not be used unless the benefit outweighs the risk. The mother should be informed about the risk to the fetus. If treatment with bendamustine hydrochloride is absolutely necessary during pregnancy or if pregnancy occurs during treatment, the patient should be informed about the risks for the unborn child and be monitored carefully. The possibility of genetic counseling should be considered.
Breast-feeding
It is not known whether passes into the breast milk, therefore, bendamustine hydrochloride is contraindicated during breast-feeding (see Contraindications). Breast-feeding must be discontinued during treatment with bendamustine hydrochloride.
Fertility
Men being treated with are advised not to father a child during and for up to 6 months following cessation of treatment. Advice on conservation of sperm should be sought prior to treatment because of the possibility of irreversible infertility due to therapy with bendamustine hydrochloride.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. However, ataxia, peripheral neuropathy and somnolence have been reported during treatment with bendamustine hydrochloride (see Adverse Reactions). Patients should be instructed that if they experience these symptoms they should avoid potentially hazardous tasks such as driving and using machines.

4.8 Undesirable effects
The most common adverse reactions with bendamustine hydrochloride are hematological adverse reactions (leukopenia, thrombopenia), dermatologic toxicities (allergic reactions), constitutional symptoms (fever), gastrointestinal symptoms (nausea, vomiting).
The table below reflects the data obtained with bendamustine hydrochloride in clinical trials.

MedDRA system organ class	Very common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1000 to <1/100	Rare ≥1/10000 to <1/1000	Very rare <1/10000	Not known (cannot be estimated from the available data)
Infections and Infestations	Infection NOS*			Sepsis	Pneumonia primary atypical	
Neoplasm benign, malignant		Tumor lysis syndrome				
Blood and lymphatic system disorders	Leukopenia NOS*, Thrombo-cytopenia	Hemorrhage, Anemia, Neutropenia			Hemolysis	
Immune system disorders		Hyper-sensitivity NOS*		Anaphylactic reaction, Anaphylactoid reaction	Anaphylactic shock	
Nervous system disorders		Insomnia		Somnolence, Aphonia	Dysgeusia, Paresthesia, Peripheral sensory neuropathy, Anticholinergic syndrome, Neurological disorders, Ataxia, Encephalitis	
Cardiac disorders		Cardiac dysfunction, such as palpitations, angina pectoris, Atrial fibrillation	Pericardial effusion		Tachycardia, Myocardial infarction, Cardiac failure	

Vascular disorders		Hypotension		Acute Circulatory failure	Phlebitis	
Respiratory, thoracic and mediastinal disorders		Pulmonary dysfunction			Pulmonary fibrosis	
Gastro-intestinal disorders	Nausea, vomiting	Diarrhea, Constipation, Stomatitis				Hemorrhagic esophagitis, Gastrointestinal hemorrhage
Skin and subcutaneous tissue disorders		Alopecia, Skin disorders NOS*		Erythema, Dermatitis, Pruritus, Maculopapular rash, Hyperhidrosis		
Reproductive system and breast disorders		Amenorrhea			Infertility	
General disorders and administration site conditions	Mucosal inflammation, Fatigue, Pyrexia	Pain, Chills, Dehydration, Anorexia			Multi-organ failure	
Investigations	Hemoglobin decrease, Creatinine increase, Urea increase	AST increase, ALT increase, Alkaline phosphatase increase, Bilirubin increase, Hypokalemia				

NOS* = Not otherwise specified
A small number of cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in patients some using in combination with allopurinol or in combination with allopurinol and rituximab. In addition, a few cases of hepatitis B reactivation resulting in hepatic failure have been reported in patients treated with. Pancytopenia, headache, dizziness, opportunistic infection (e.g. herpes zoster, cytomegalovirus, pneumocystis jirovecii pneumonia), bone marrow failure, hepatic failure, renal failure, nephrogenic diabetes insipidus, drug reaction with eosinophilia and systemic symptoms (combination therapy with rituximab) have also been reported in patients treated with .

The CD4/CD8 ratio may be reduced. A reduction of the lymphocyte count was seen. In immunosuppressed patients, the risk of infection (e.g., with herpes zoster) may be increased.
There have been isolated reports of necrosis after accidental extra-vascular administration, tumor lysis syndrome, and anaphylaxis.
The risk of myelodysplastic syndrome and acute myeloid leukaemias is increased in patients treated with alkylating agents (including). The secondary malignancy may develop several years after chemotherapy has been discontinued.

4.9 Overdose
After application of a 30-minute infusion of once every 3 weeks, the maximum tolerated dose (MTD) was 280 mg/m^2. Cardiac events of CTC grade 2 occurred, which were compatible with ischemic ECG changes that were regarded as dose limiting.
In a subsequent study with a 30-minute infusion of at day 1 and 2 every 3 weeks, the MTD was found to be 180 mg/m^2. The dose limiting toxicity was grade 4 thrombocytopenia. Cardiac toxicity was not dose limiting with this schedule.
Counter measures
There is no specific antidote. Bone marrow transplantation and transfusions (platelets, concentrated erythrocytes) may be made or hematological growth factors may be given as effective countermeasures to control hematological side effects.
Bendamustine hydrochloride and its metabolites are dialyzable to a small extent.

5. Pharmacological Properties.
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Antineoplastic agents, alkylating agents
ATC code: L01AA09
Bendamustine hydrochloride is an alkylating antitumor agent with unique activity containing a purine-like benzimidazole ring. The antineoplastic and cytocidal effect of is based essentially on a cross-linking of DNA single and double strands by alkylation. As a result, DNA matrix functions and DNA synthesis and repair are impaired is active against both quiescent and dividing cells.
The exact mechanism of action of remains unknown.
The antitumor effect of bendamustine hydrochloride has been demonstrated by several in-vitro studies in different human tumor cell lines (breast cancer, non-small cell and small cell lung cancer, ovary carcinoma and different leukemia) and in-vivo in different experimental tumor models with tumors of mouse, rat and human origin (melanoma, breast cancer, sarcoma, lymphoma, leukemia and small cell lung cancer).
Bendamustine hydrochloride showed an activity profile in human tumor cell lines different to that of other alkylating agents. The active substance revealed no or very low cross-resistance in human tumor cell lines with different resistance mechanisms at least in part due to a comparatively persistent DNA interaction. Additionally, it was shown in clinical studies that there is no complete cross-resistance of with anthracyclines,