**Generic name:** bendamustine hydrochloride (pronounced ben-da-MUS-teen)

**Trade name(s):** Treanda®; Bendeka® by Teva; Belrapzo® by Eagle Pharmaceuticals

Note: In 2016, Teva replaced Treanda® with Bendeka® citing the following two reasons:
- Bendeka® has a shorter infusion time than Treanda® (10 minutes versus 30-60 minutes).
- Bendeka® is compatible with certain chemicals contained in some infusion equipment, and Treanda® is not.

Both Bendeka® and Treanda® contain bendamustine hydrochloride and have the same indications for use. Treanda® is still available through Cephalon, Inc., a subsidiary of Teva.

**Drug type:** Bendamustine is an anti-cancer chemotherapy drug that is classified as an alkylating agent.

**What conditions are treated by bendamustine?**

Bendamustine is FDA-approved for the treatment of people with chronic lymphocytic leukemia (CLL) and indolent (slow-growing) B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab (Rituxan®) or a rituximab-containing regimen.

Waldenstrom macroglobulinemia (WM) is a type of indolent B-cell NHL. Bendamustine combined with the monoclonal antibody rituximab is one of four therapy regimens preferred by the WM experts of the National Comprehensive Cancer Network (NCCN®) – an alliance of 31 leading cancer centers in the U.S. – and those who participated at the tenth International Workshop for Waldenstrom Macroglobulinemia (IWWM-10). While the bendamustine/rituximab combination regimen is preferred, using bendamustine alone is recommended for people who cannot take rituximab.

These two protocols – bendamustine in combination with rituximab, and bendamustine alone for patients who are rituximab-intolerant – are preferred regimens for both initial (also called first-line or primary) treatment of WM, as well as for previously treated WM.

**What are some of the benefits and risks of treatment with bendamustine?**

Bendamustine regimens are particularly useful for people who have enlarged lymph nodes, livers, or spleens, or when a rapid response to treatment is needed. Another advantage is that it’s used for a fixed duration of time – not as an ongoing, lifetime therapy. Additionally,
bendamustine is not contraindicated in potential candidates for autologous stem cell transplant (ASCT), as it’s unlikely to affect stem cell collection.

A possible disadvantage of bendamustine is that approximately 1 percent of people who were treated with this drug developed a secondary cancer like leukemia. It is not known if bendamustine caused this effect; people with WM may also develop secondary cancers that are not related to drug treatments.

Your physician will consider many factors when recommending a therapy, including your symptoms, genomic profile, preferences, insurance coverage, other chronic health issues, and safety profile of the regimen. Discuss these things with your doctor during the treatment decision making process.

**How is bendamustine given?**

Bendamustine is given as an intravenous (IV) infusion into a vein through a small needle in your arm. There is no pill form of bendamustine. Your doctor will determine the appropriate dose and schedule of bendamustine based on several factors including your height, weight, blood counts, and any specific medical issues you may have.

Bendamustine may be administered at a doctor’s office, the hospital, or an infusion center. Tell your nurse if you have any pain, burning, redness, swelling, or fluid leaking around the IV insertion site, as this drug may cause tissue damage if it leaks out of your vein into the surrounding skin.

**How does bendamustine work?**

Normal healthy cells divide and grow in a precise, orderly way. Cancer cells, however, no longer have the normal mechanisms in place that control and limit cell division, resulting in rapid and uncontrollable growth.

All chemotherapy drugs interfere with a cancer cell’s ability to grow or multiply. Many drugs attack cancer cells by interacting with the cell’s genetic makeup (RNA or DNA) in such a way that they kill the cancer cell or prevent it from growing or dividing. Alkylating agents, like bendamustine, work by damaging the DNA of cells.

**What are the side effects of bendamustine?**

Chemotherapy is most effective at killing cells that divide rapidly, which is why they work against WM cells. However, there are healthy cells in the body that divide quickly as well. They exist in the bone marrow (where new blood cells are made); line the mouth, stomach and bowel; and grow hair. Damage to these healthy cells is what causes some of the common side
effects of chemotherapy – resulting in low blood counts, mouth sores, nausea, diarrhea, and/or hair thinning, respectively. Fortunately, the normal cells will grow back and most associated side effects will go away once treatment ends.

The most common side effects of bendamustine include the following: fatigue, fever, nausea and vomiting, diarrhea, constipation, loss of appetite, cough, headache, weight loss, difficulty breathing, rash, mouth irritation, low red blood cells (oxygen-carrying cells), low platelets (blood-clotting cells), and decreased number of three different types of white blood cells (infection-fighting cells). Most people will not have all of these side effects. If you experience any side effect, tell your healthcare provider. There are medications and strategies that can help lessen their severity.

**When should a healthcare provider be contacted right away?**

Even though it may be rare, some people may have serious side effects when taking bendamustine. Inform your doctor right away if you have any of the following signs or symptoms, as you may need immediate medical attention:

- Signs of an allergic reaction like a rash, itching, and hives; blistered or peeling skin; tightness in the chest or throat; trouble breathing, swallowing, or talking.
- Signs of infection like fever, chills, cough, and wounds that won’t heal.
- Signs of bleeding like throwing up blood; blood in your urine; or black, red, or tarry stools.
- Signs of dehydration like dizziness; confusion; extreme fatigue, muscle pain or weakness; unable to pass urine; or a heartbeat that doesn’t feel normal.
- Signs of liver problems like dark urine; light-colored stools; upset stomach, throwing up, or stomach pain; yellow skin or eyes.
- Signs of a rare but serious complication called tumor lysis syndrome, which occurs when large numbers of cancer cells are rapidly killed by the therapy. These cells release uric acid, potassium, and phosphorus into the bloodstream, which can lead to kidney failure. Tumor lysis syndrome usually occurs within 24-48 hours of therapy. Your doctor will prescribe fluids to keep you well-hydrated, and you may be given a drug called allopurinol that blocks uric acid production. Call your doctor right away if you have a fast or abnormal heartbeat; muscle weakness or cramps; trouble passing urine; upset stomach, throwing up, diarrhea; or feel extremely sluggish.

These are not all the side effects that can occur with bendamustine. In general, it’s always good practice to inform your healthcare provider if you experience any unusual symptoms. Some serious side effects may require changes in therapy, such as lowering the dose given, waiting longer between doses, or stopping the use of the drug.

**What are some self-care tips while taking bendamustine?**
The following are some things you need to do or know while taking this drug. Before starting treatment with bendamustine, tell your doctor about:

- All other medicines you are taking, including prescription, over-the-counter (OTC), vitamins, and supplements.
- Any allergies you have to drugs, foods, or substances (like latex for example).
- Health problems you may have, particularly kidney or liver disease.
- Whether you are, or may be, pregnant. This drug may cause harm to an unborn baby. A pregnancy test will be done before you start bendamustine to make sure you are not pregnant.
- Your desire to father a child. Bendamustine may impair fertility in some men; this may resolve after treatment, may last several years, or may be permanent. Discuss this with your doctor.
- Whether you are breastfeeding. You cannot breastfeed while taking this drug and for one week after your last dose.

While taking bendamustine:

- Try to drink at least two to three quarts of fluid every 24 hours (particularly the 24 hours before and 48 hours following the infusion), unless you are instructed otherwise.
- You may be at risk of infection so try to avoid crowds or people with infections, colds, or flu and wash your hands often.
- You may bleed more easily. Avoid contact sports or activities that could cause injury. Use an electric razor and a soft toothbrush to minimize bleeding.
- To help prevent/treat mouth sores, use a soft toothbrush and rinse three times a day with 1 teaspoon of baking soda mixed with 8 ounces of water.
- To reduce nausea, take anti-nausea medications as prescribed by your doctor and eat small, frequent meals. In general, drinking alcoholic beverages should be kept to a minimum or avoided completely.
- While taking bendamustine, do not take aspirin or products containing aspirin unless your doctor specifically permits this.
- If you or your sex partner may get pregnant, use birth control while taking this drug and for some time after the last dose. Bendamustine may cause fetal harm. Ask your doctor how long to use birth control.

How will I be monitored while taking bendamustine?

You will be checked regularly by your doctor to monitor side effects and assess your response to therapy. Periodic blood work will be obtained to monitor your blood counts and evaluate the function of organs, such as your liver and kidneys.

Acknowledgments
The IWMF acknowledges the important contributions to treatment guidelines made by the National Comprehensive Cancer Network and the International Workshops on Waldenstrom Macroglobulinemia.

The IWMF also acknowledges Dr. Castillo for medical review of this publication.

About the IWMF
The International Waldenstrom’s Macroglobulinemia Foundation (IWMF) is a patient-founded and volunteer-led, nonprofit 501(c)(3) organization with an important vision, “a world without WM,” and a mission to “support and educate everyone affected by WM while advancing the search for a cure.”

More information about Waldenstrom macroglobulinemia and the services and support offered by the IWMF and its affiliate organizations can be found on our website, www.iwmf.com. The IWMF relies on donations to continue its mission, and we welcome your support. The Foundation maintains a business office at 6144 Clark Center Ave., Sarasota, FL 34238. The office can be contacted by phone at 941-927-4963, by fax at 941-927-4467, or by email at info@iwmf.com.

The information presented here is intended for educational purposes only. It is not meant to be a substitute for professional medical advice. Patients should use the information provided herein in consultation with, and under the care of, a professional medical specialist with experience in the treatment of WM.

Copyright© The International Waldenstrom’s Macroglobulinemia Foundation September 2021