VELCADE® (bortezomib) is approved for the treatment of patients with multiple myeloma (a cancer of the plasma cells). VELCADE is also approved for the treatment of patients with mantle cell lymphoma (a cancer of the lymph nodes) who have already received other treatments.

Before you receive treatment with VELCADE, tell your doctor about all of your medical conditions. You should not receive VELCADE if you are allergic to bortezomib, boron, or mannitol. VELCADE must not be administered into your spinal fluid (intrathecally).

Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.
Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.
How to use this guide

This guide is designed to help you learn more about relapsed mantle cell lymphoma and its treatment with VELCADE® (bortezomib). You may also want to share this guide with your family and friends, as it contains resources that may be helpful.

This guide will provide you with information on:

▼ Relapsed mantle cell lymphoma
▼ Understanding VELCADE (bortezomib)
▼ Possible side effects and important safety information
▼ VELCADE Patient Assistance Program (PAP)
▼ Record keeping
▼ Helpful terms
▼ Support and resources

Please keep in mind that this guide is not intended to replace conversations with your healthcare team. Your doctor and other healthcare providers are the most valuable resources for answering questions about mantle cell lymphoma and treatment with VELCADE.
What is relapsed mantle cell lymphoma?

Relapsed *mantle cell lymphoma* is the return of mantle cell lymphoma after previous treatment.

Mantle cell lymphoma is a type of blood cancer that affects *white blood cells* called *lymphocytes*. It gets its name because it affects lymphocytes in the *mantle zone* of a lymph node. A rare form of *non-Hodgkin lymphoma* (NHL), mantle cell lymphoma makes up about 6% of all NHL cases in the United States. It is most common in middle-aged or older adults.

Lymphocytes are white blood cells that help fight infections and other diseases in the body. They are found mostly in the *lymphatic system*, which includes your *bone marrow*, spleen, and lymph nodes. When lymphocytes become cancerous, they can multiply and spread to many parts of the body and form tumors. These tumors can cause the lymph nodes, as well as the spleen, to enlarge.

Mantle cell lymphoma is considered to be an aggressive cancer, meaning it can grow and spread rapidly. At the time of diagnosis, it is common for mantle cell lymphoma to have already spread to other parts of the body.

Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.

*Find definitions of terms in italic on page 22.*
How relapsed mantle cell lymphoma may affect you

Watch for common symptoms of mantle cell lymphoma that may indicate a *relapse*, or return, of the disease. Symptoms may include:

- Swollen glands, lymph nodes, and tonsils
- Fever
- Night sweats
- Loss of appetite
- Feeling tired
- Weight loss
- Nausea and/or vomiting
- Indigestion
- Abdominal pain or bloating
- Feeling of fullness
- Pressure or pain in lower back, often extending down one or both legs

These symptoms could also be signs of other medical problems. Talk with your doctor about any symptoms or questions you may have.
What is VELCADE?

The Food and Drug Administration (FDA) approved VELCADE (bortezomib) in 2003. VELCADE is a targeted therapy called a proteasome inhibitor.

VELCADE is approved for the treatment of patients with mantle cell lymphoma (a cancer of the lymph nodes) who have already received at least 1 other treatment.

How does VELCADE work?

As a targeted therapy, VELCADE works by blocking or slowing down the action of proteasomes (PROH-tee-ays-oms) inside cells. Proteasomes break down proteins in both healthy and cancerous cells.

When proteasome activity is blocked or slowed down, proteins in the cells build up. This creates an imbalance of proteins that may cause cells to stop growing, dividing, and multiplying. Cancer cells divide and multiply more rapidly than most other cells. The goal of treatment with VELCADE is to target these rapidly dividing cells and stop them from thriving and multiplying.
How is VELCADE given?

Like many cancer medications, VELCADE is given in cycles. A cycle of therapy usually includes the weeks when you will receive the drug and the week(s) you will rest and not receive the drug. The number of cycles you will receive depends on several factors, including how well you respond to treatment and whether side effects occur. Your doctor will discuss your treatment plan with you.

Your doctor will also decide the best way to give you VELCADE. It may be administered in one of two ways. It can be given as a *subcutaneous* or *intravenous* (IN-truh-VEE-nus) injection. When VELCADE is administered subcutaneously, it is injected under the skin. When VELCADE is administered intravenously, it is injected into a vein for 3 to 5 seconds. Both ways are administered in a doctor’s office or at a clinic.
What are clinical trials?

*Clinical trials* are studies in which patients volunteer to test medical treatments. Doctors use clinical trials to learn whether a new drug works and is safe for patients, or whether an existing drug can be used in new ways. These studies provide the necessary evidence for the FDA to approve the use of treatment for a specific disease.

**VELCADE for patients with relapsed mantle cell lymphoma**

Based on a large clinical trial of 155 patients with *mantle cell lymphoma* who had been treated for it before, VELCADE (bortezomib) was approved by the FDA in mantle cell lymphoma for patients who have already received at least 1 treatment.

In this clinical trial, 31% of patients responded to treatment with VELCADE.

In the same clinical trial, the most commonly reported side effects in patients with relapsed mantle cell lymphoma were numbness, tingling, burning, or weakness in hands or feet; fatigue (tiredness); diarrhea; nausea; constipation; vomiting; and rash.

In this trial, 23% of patients stopped treatment with VELCADE due to side effects. The most commonly reported serious adverse reactions were nausea, vomiting, abdominal pain, fainting, fever, pneumonia, and sepsis (infection in the blood or tissues).

Every patient’s experience with any medication may vary. Your results with VELCADE may differ from those seen in clinical trials. Talk to your doctor about any concerns you have about your therapy. For more information on side effects, please see pages 12–15.
VELCADE® (bortezomib) treatment for patients with relapsed mantle cell lymphoma

For patients with relapsed mantle cell lymphoma, treatment may be given for a median of 8 cycles (24 weeks). Each cycle lasts 3 weeks. Eight treatment cycles will last about 6 months. Your doctor will discuss your treatment plan with you.

Recommended treatment schedule

VELCADE (bortezomib) is given in 3-week (21-day) cycles. You would receive VELCADE twice per week in weeks 1 and 2, followed by a 10-day rest period. At the end of this rest period, the next cycle begins.

▼ Eight cycles of treatment will last about 6 months.

For extended therapy (more than 8 cycles), you may be given VELCADE once per week for 4 weeks, followed by a 13-day rest period (maintenance schedule). Or you may be given VELCADE on a standard schedule of twice per week, as shown in the calendars on the right.

Your doctor will discuss your treatment plan with you.

Your doctor will also discuss which way of receiving VELCADE—subcutaneously or IV—is best for you. The dosing schedule is the same for both.

Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.

Find definitions of terms in italic on page 22.
Cycles 1–8

**TWICE WEEKLY, 3-WEEK CYCLES**

1 2 3 4 5 6 7
8 9 10 11 12 13 14
15 16 17 18 19 20 21

**for extended therapy**

Cycle 9 and beyond

**WEEKLY MAINTENANCE SCHEDULE**

1 2 3 4 5 6 7
8 9 10 11 12 13 14
15 16 17 18 19 20 21
22 23 24 25 26 27 28
29 30 31 32 33 34 35

**OR**

**TWICE-WEEKLY STANDARD SCHEDULE**

1 2 3 4 5 6 7
8 9 10 11 12 13 14
15 16 17 18 19 20 21

Twice-weekly, 3-week cycles are repeated 8 times.
What is VELCADE used for?
VELCADE (bortezomib) is approved for the treatment of patients with multiple myeloma (a cancer of the plasma cells). VELCADE is also approved for the treatment of patients with mantle cell lymphoma (a cancer of the lymph nodes) who have already received other treatments.

How is VELCADE administered?
VELCADE is prescribed by a physician experienced in the use of medications to treat cancer. It is administered by a healthcare professional as an injection into your vein (intravenously, or IV) or under your skin (subcutaneously). VELCADE must not be administered into your spinal fluid (intrathecally).

Who should not receive VELCADE?
Before you receive treatment with VELCADE, tell your doctor about all of your medical conditions. You should not receive VELCADE if you are allergic to bortezomib, boron, or mannitol.

What are the possible side effects of VELCADE?
VELCADE can cause serious side effects, including:

▼ Peripheral neuropathy. VELCADE can cause damage to the nerves, a condition called peripheral neuropathy. You may feel muscle weakness, tingling, burning, pain, and loss of feeling in your hands and feet, any of which can be severe. Tell your doctor if you notice any of these symptoms. Your doctor may change the dose and/or schedule of VELCADE or stop it altogether. If you have peripheral neuropathy before starting VELCADE, your doctor could consider giving you VELCADE subcutaneously.

Please see accompanying full Prescribing Information for VELCADE, including Warnings and Precautions.
Low blood pressure. VELCADE can cause a drop in blood pressure. Tell your doctor if you have low blood pressure, feel dizzy, or feel as though you might faint. If you are taking drugs that lower blood pressure, your medications might need to be adjusted. If you are not drinking enough liquids, your doctor may need to administer IV fluids.

Heart problems. Treatment with VELCADE can cause or worsen heart rhythm problems and heart failure. Your doctor may closely monitor you if you have, or are at risk for, heart disease. Tell your doctor if you experience chest pressure or pain, palpitations, swelling of your ankles or feet, or shortness of breath.

Lung problems. There have been reports of lung disorders in patients receiving VELCADE. Some of these events have been fatal. Tell your doctor if you experience any cough, shortness of breath, wheezing, or difficulty breathing.

Liver problems. If you have liver problems, it can be harder for your body to get rid of VELCADE. VELCADE has caused sudden liver failure in patients who were taking many medications or had other serious medical conditions. Symptoms of liver problems include a yellow discoloration of the eyes and skin (jaundice) and changes in liver enzymes measured in blood tests. Your doctor will closely monitor you if you have liver disease.

Posterior reversible encephalopathy syndrome (PRES). There have been reports of a rare, reversible condition involving the brain, called PRES, in patients treated with VELCADE. Patients with PRES can have seizures, high blood pressure, headaches, tiredness, confusion, blindness, or other vision problems. Treatment with VELCADE should be stopped in cases of PRES.

(continued)
Important Safety Information
for VELCADE® (bortezomib)

▼ **Gastrointestinal problems.** VELCADE (bortezomib) treatment can cause nausea, vomiting, diarrhea, and constipation. If your symptoms are severe, your doctor may recommend IV fluids and/or medications.

▼ **Neutropenia (low levels of neutrophils, a type of white blood cell).** VELCADE can cause low levels of white blood cells (infection-fighting cells). If your white blood cells become low, you can be at higher risk for infections. Tell your doctor if you develop a fever or believe you have an infection.

▼ **Thrombocytopenia (low levels of platelets).** VELCADE can cause low levels of platelets (clot-forming cells). If platelets become very low, there is an increased risk of bleeding. Your doctor may recommend a platelet transfusion.

You will have regular blood tests to check your cell counts during your treatment with VELCADE. If the number of these cells is very low, your doctor may change the dose and/or schedule of VELCADE.

▼ **Tumor lysis syndrome (TLS).** TLS is a syndrome that causes a chemical imbalance in the blood that could lead to heart and/or kidney problems. TLS can occur with cancer treatments, and your doctor will be monitoring your blood and urine for any signs of this syndrome. If you develop TLS, your doctor will take appropriate steps to treat it.

More than 1 in 5 patients (20%) receiving VELCADE have experienced the following side effects: nausea, diarrhea, thrombocytopenia, neutropenia, peripheral neuropathy, fatigue, neuralgia (nerve pain), anemia, leukopenia (low levels of white blood cells), constipation, vomiting, lymphopenia (low levels of a certain type of white blood cells), rash, pyrexia (fever), and anorexia.
What other information should you discuss with your doctor?

Women should avoid becoming pregnant or breast-feeding while being treated with VELCADE. Discuss with your doctor when it is safe to restart breast-feeding after finishing your treatment.

You should also tell your doctor if you:

▼ Have kidney disease. If you are on dialysis, your doctor will administer VELCADE after the dialysis procedure.

▼ Are taking medication for diabetes. VELCADE can affect your blood glucose levels. Your doctor may require close monitoring of your blood glucose levels and change the dose of your diabetes medicine while you are being treated with VELCADE.

▼ Have liver disease.

▼ Are using any other medications, including prescription and over-the-counter drugs, herbal or dietary supplements, or holistic treatments. St. John’s wort should be avoided.

▼ Develop a rash of any type while receiving VELCADE.

The side effects of VELCADE may impair your ability to drive or operate machinery.

These are not all of the possible side effects with VELCADE. It is important to always contact your doctor if you experience any side effects while on VELCADE. If you have any questions about VELCADE, contact your doctor. Additional information is available on the Web site VELCADE.com.

Please see accompanying full Prescribing Information for VELCADE, including Warnings and Precautions.
Paying for treatment with VELCADE® (bortezomib)

If you have questions about paying for treatment with VELCADE, we may have the answers

Millennium Pharmaceuticals, Inc., distributor of VELCADE (bortezomib), may be able to help you, your caregivers, and your healthcare team with the reimbursement process.

Millennium may also be able to help with the cost of VELCADE through its Patient Assistance Program. This program can help in several ways:

▶ Provide a counselor to talk about insurance coverage and verification.

▶ Find support for appealing a claim.*

▶ Identify alternative and supplemental insurance coverage options.

▶ Find co-payment foundation support information.

To apply for the Patient Assistance Program, find out about eligibility, or ask general questions about paying for treatment with VELCADE, contact us at:

1-866-VELCADE (835-2233), option 2,
Monday through Friday, 8 AM to 8 PM ET,
or VELCADEassist.com

Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.

Find definitions of terms in italic on page 22.

*The VELCADE Patient Assistance Program does not file claims or appeal claims for callers. It also cannot guarantee that you will be successful in obtaining reimbursement.
We recommend using this space to help keep track of:

▼ Your medical appointments and checkups
▼ Your test results
▼ Questions to ask your doctor

Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.
Bone marrow: (BOHN-MAYR-oh) The spongy inner part of the bones where blood cells are made.

Clinical trials: The testing of a new medical treatment on a limited population with a given diagnosis; helps to determine if the treatment is safe and effective enough to be offered to the larger population with that disease. Clinical trials are often done in phases.

Gastrointestinal problems: (gas-trow-in-TES-tuh-nl) Include nausea, diarrhea, constipation, and vomiting.

Intravenous (IV): (in-truh-VEE-nuhs) Into a vein.

Lymphatic system: (lim-FAH-tik SIS-tem) A system of tissues and organs, including the bone marrow, spleen, and lymph nodes. It is part of our immune system, and among other functions, it produces, stores, and carries white blood cells that fight infections and other diseases.

Lymphocyte: (LIM-fow-syt) A white blood cell responsible for immune protection.

Mantle cell lymphoma: (MAN-tul sel lim-FOH-muh) A type of cancer seen in the lymph nodes, spleen, bone marrow, blood, and gastrointestinal system.

Mantle zone: An outer region in a central part of a lymph node where lymphocytes are found.

Neutrophil: (NOO-trow-nil) A type of white blood cell that helps to fight infection.

Non-Hodgkin lymphoma: (nawn-HOJ-kin lim-FOW-muh) Any of a large group of cancers of lymphocytes (white blood cells) that lack characteristics of Hodgkin lymphoma.

Proteasome: (PRO-tee-uh-zohm) A part of a cell that breaks down unneeded proteins.

Proteasome inhibitor: A drug that blocks the action of proteasomes.

Relapse: The return of a disease or symptoms after apparent recovery.

Subcutaneous: (sub-kyew-TAY-nee-es) Under the skin.

White blood cells: Formed mainly in the bone marrow, these cells help protect the body from infection and disease.
Helpful resources

Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.

This list includes just some of the organizations that offer support and resources to people with mantle cell lymphoma. It is meant for informational purposes only and is not meant to replace your doctor’s medical advice.

- **American Cancer Society**
  - 1-800-227-2345
  - www.cancer.org

- **Association of Cancer Online Resources**
  - 1-212-226-5525
  - www.acor.org

- **Cancer Care, Inc.**
  - 1-800-813-HOPE (1-800-813-4673)
  - www.cancercare.org

- **Cancer Legal Resource Center**
  - 1-866-THE-CLRC (1-866-843-2572)
  - www.cancerlegalresourcecenter.org

- **Cancer Support Community**
  - 1-888-793-9355
  - www.cancersupportcommunity.org

- **The Leukemia & Lymphoma Society (LLS)**
  - 1-800-955-4572
  - www.lls.org

- **Lymphoma Research Foundation**
  - 1-800-500-9976
  - www.lymphoma.org

- **Medicare**
  - 1-800-MEDICARE (1-800-633-4227)
  - www.medicare.gov

- **National Cancer Institute**
  - 1-800-4-CANCER (1-800-422-6237)
  - www.cancer.gov

- **National Coalition for Cancer Survivorship (NCCS)**
  - 1-888-650-9127
  - www.canceradvocacy.org

- **National Organization for Rare Disorders (NORD)**
  - 1-203-744-0100
  - www.rarediseases.org
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www.rarediseases.org
Resources for VELCADE® (bortezomib)
1-866-VELCADE (835-2233), option 2
Use this toll-free line to talk directly with a medical information specialist who can provide:

▼ Help with paying for treatment*
▼ Healthcare provider and caregiver resource information

For more information about VELCADE (bortezomib), please visit VELCADE.com.

Please see Important Safety Information for VELCADE on pages 12–15 and accompanying full Prescribing Information.

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Please see full Prescribing Information at

velcade.com/Files/PDFs/VELCADE_PREScribing_INFORMATION.pdf