

**Re: A New Route of Administration for VELCADE Is Now Available**

Dear Patients and Caregivers:

Millennium: The Takeda Oncology Company is pleased to announce that the US Food and Drug Administration (FDA) has approved a new way to receive VELCADE® (bortezomib) for the treatment of multiple myeloma and relapsed mantle cell lymphoma. This approval was based on a large, international clinical trial that studied VELCADE injected under the skin (also known as subcutaneous) compared with VELCADE injected into a vein (also known as IV or intravenous). The 222 patients in this study had been treated for their myeloma and relapsed.

Please read on to learn more about the results of this trial. Also, ask your doctor about the benefits VELCADE may have for you.

**VELCADE given under the skin was as effective as VELCADE given into a vein.**

The study showed that patients given VELCADE under the skin had similar results to patients given VELCADE into a vein. The results were based on the overall response rate at 12 weeks. Additional clinical measurements from the trial are shown below.

**CLINICAL MEASUREMENTS: SUBCUTANEOUS AND IV**

	Subcutaneous (n=148)	IV (n=74)
<b>Overall Response Rate</b> (at 12 weeks)	43%	42%
<b>Complete Response</b> (at 12 weeks)	7%	8%
<b>Time to Progression</b>	10.4 months	9.4 months
<b>Progression-Free Survival</b>	10.2 months	8.0 months

**Overall response rate** is the percentage of patients whose disease showed a measurable improvement.

**Complete response** is the disappearance of all signs of cancer in response to treatment.

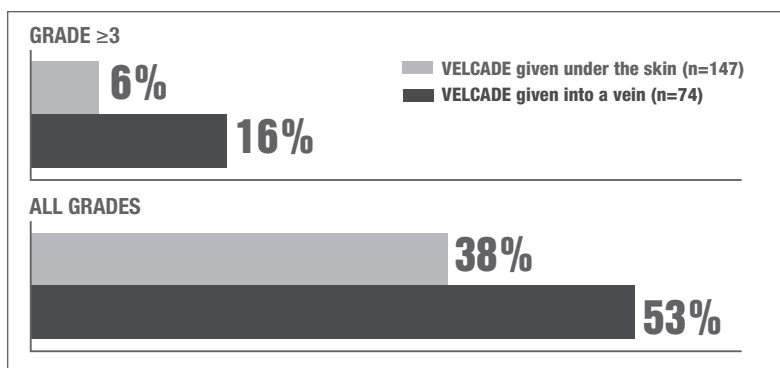
**Time to progression** is the time from study entry, or diagnosis, until a patient shows signs of disease progression.

**Progression-free survival** is the time from study entry to the first sign of disease progression or death, whichever comes first.

**Difference in incidence of peripheral neuropathy with VELCADE given under the skin.**

The overall safety of VELCADE was similar between patients receiving it under the skin and patients receiving it in a vein. However, there were differences in the rate of peripheral neuropathy, shown in the graph below.

**DIFFERENCE IN THE RATE OF PERIPHERAL NEUROPATHY**



▼ A condition that occurs due to damage to the peripheral nerves of the arms, hands, legs, and feet. Symptoms include numbness, tingling, pain, itching, and a “pins and needles” sensation. Can also lead to weakness and loss of function

▼ Patients should tell their doctor if they have any of these symptoms. The doctor may change the dose and/or schedule of VELCADE, or stop it completely.

▼ For patients who have peripheral neuropathy before starting VELCADE, their doctor could consider giving VELCADE under the skin.

**Important Safety Information for VELCADE**

**What is VELCADE used for?**

VELCADE 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.

- **Low blood pressure.** VELCADE® (bortezomib) 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 disorders.** 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 disease.** 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. In patients with moderate or severe liver disease, VELCADE should be started at a lower dose. Additional dose adjustments may be made based on your tolerance of the drug.
- **Gastrointestinal problems.** VELCADE 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) and thrombocytopenia (low levels of platelets).** VELCADE can cause low levels of white blood cells (infection-fighting cells) and/or platelets (clot-forming cells). 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. 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. If platelets become very low, there is an increased risk of bleeding. Your doctor may recommend a platelet transfusion. There have been cases of bleeding in the stomach, bowels, and brain during treatment with VELCADE.
- **Tumor lysis syndrome (TLS).** 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.
- **Reversible posterior leukoencephalopathy syndrome (RPLS).** There have been reports of a rare, reversible condition involving the brain, called RPLS, in patients treated with VELCADE. Patients with RPLS can have seizures, high blood pressure, headaches, tiredness, confusion, blindness, or other vision problems. Treatment with VELCADE should be stopped in cases of RPLS.

More than 30% of patients receiving VELCADE have experienced the following side effects: thrombocytopenia, neutropenia, nausea, peripheral neuropathy, neuralgia (nerve pain), pyrexia (fever), diarrhea, anemia, leukopenia (low levels of white blood cells), decreased appetite, fatigue, constipation, vomiting, dehydration, dyspnea (difficulty breathing), cough, asthenia (low energy), insomnia (trouble sleeping), peripheral edema (swelling of the limbs), and headache.

#### What other information should you discuss with your doctor?

Women should avoid becoming pregnant or breastfeeding while being treated with VELCADE. Discuss with your doctor when it is safe to restart breastfeeding 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 medicines like ketoconazole (an antifungal), ritonavir (an antiviral), and rifampin (an antibiotic), which will require close monitoring during treatment with VELCADE.
- Are using any other medications (including 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 website [www.VELCADE.com](http://www.VELCADE.com).

**Please see the accompanying full prescribing information for VELCADE, including warnings and precautions. It is also available at [VELCADE.com](http://VELCADE.com).**

Please visit [VELCADE.com](http://VELCADE.com) to learn more about the potential benefits of receiving VELCADE under the skin.



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**Please see full Prescribing Information at**

**[velcade.com/Files/PDFs/VELCADE PRESCRIBING INFORMATION.pdf](http://velcade.com/Files/PDFs/VELCADE_PRESCRIBING_INFORMATION.pdf)**