

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrVELCADE® bortezomib for Injection

Read this carefully before you start taking **Velcade** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Velcade**.

Your cancer will be treated with Velcade. You may also receive other medications including melphalan and prednisone. Read information geared to the patient for these medications as well as this one.

Serious Warnings and Precautions

- Velcade will be given to you under the supervision of a physician qualified in the use of anti-cancer drugs.
- If you are given too much Velcade, it can lead to death.

Serious side effects that may occur with Velcade include:

- Low blood pressure and other serious heart disorders
- Bleeding into the brain or gastrointestinal tract (stomach or bowel)
- Severe motor neuropathy, which is muscle weakness due to nerve damage
- Acute diffuse infiltrative pulmonary disease. This is a lung disease, where the lung is inflamed or scarred.

What is Velcade used for?

Velcade is used to treat of adults with multiple myeloma that has:

- not been treated previously. These patients may or may not be able to have a stem cell transplant. For these patients, Velcade will be given with other medicines.
- gotten worse after one or more previous treatments. These patients are considered to have relapsed multiple myeloma. They may have already had a stem cell transplant or are not able to receive one.

Velcade is also used to treat adults with mantle cell lymphoma that has:

- not been treated previously. These patients will not be able to have a stem cell transplant. For these patients Velcade will be given with other medicines; or
- gotten worse after or did not respond to one or more previous treatments. These patients are considered to have relapsed or refractory mantel cell lymphoma.

How does Velcade work?

Velcade is a chemotherapy medicine. It is used to kill cancer cells.

What are the ingredients in Velcade?

Medicinal ingredients: bortezomib mannitol boronic ester

Non-medicinal ingredients: mannitol

Velcade comes in the following dosage forms:

Powder: 3.5 mg of bortezomib (as a mannitol boronic ester).

Do not use Velcade if:

- you are allergic to bortezomib, boron or to any of the other ingredients in this medicine.

Velcade must not be given by injection into the spinal canal (intrathecal injection).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Velcade. Talk about any health conditions or problems you may have, including if you:

- have had any bleeding problems, a low level of red blood cells, platelets, or white blood cells. These conditions may become worse during treatment with Velcade;
- are suffering from diarrhea, constipation, nausea or vomiting. These may become worse during Velcade treatment;
- have any problems with your heart or blood pressure including a history of fainting, dizziness or light-headedness;
- have kidney problems;
- have liver problems;
- have had any problems in the past with numbness, tingling, or pain in the hands or feet. This is called neuropathy. It may become worse during Velcade treatment;
- have or have a history of amyloidosis. This is a condition where abnormal protein builds up in tissues;
- have shortness of breath with activity (may get progressively worse), cough, and difficulty breathing. These symptoms may develop or worsen during Velcade treatment.
- are taking drugs that cause low blood pressure,
- are dehydrated
- are taking medicines by mouth to treat diabetes.
- have a history of seizures

Other warnings you should know about:

Velcade has not been studied in children or adolescents.

Sudden death: Two cases of sudden death have been reported in clinical trials with Velcade

Oral drugs to treat diabetes: If you are also taking drugs, by mouth, to treat diabetes, check your blood sugar levels regularly while you are receiving Velcade. Call your doctor if you notice an unusual change.

Birth control, Pregnancy and breast-feeding:

Female patients:

- If you are pregnant, able to get pregnant or think you are pregnant, there are specific risks you should discuss with your healthcare professional.
- Avoid becoming pregnant during your treatment with Velcade. It may harm your unborn baby or make you lose the pregnancy.
- If you do become pregnant, or think you are pregnant, while you are receiving Velcade, tell your healthcare professional right away.
- It is not known if Velcade passes into breastmilk. Do not breast-feed while you are receiving Velcade. If you wish to restart breast-feeding after your Velcade treatment, talk to your healthcare professional. They will tell you when it is safe to do so.

Male and female patients:

- You must use effective birth control while receiving Velcade. Continue this method of birth control or 3 months after your last dose.
- Velcade may affect your fertility. This means it may be difficult for you to have a baby in the future. Talk to your healthcare professional if you have questions about this.

Driving and using machines:

Velcade might cause fatigue, dizziness, fainting, low blood pressure or blurred vision. Do not drive or operate any dangerous tools or machines if you experience such side effects. Even if you have not felt these effects, you must still be cautious.

Tests: You will have scans of your chest before you start treatment. As well, you will have blood tests done before each dose of Velcade is given. The results of these tests will tell your healthcare professional how Velcade is affecting your blood.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Velcade:

- medicines to treat diabetes that are taken by mouth;
- medicines used to treat bacterial, viral or fungal infections including rifampicin, ritonavir and ketoconazole;
- medicines used to treat seizures including carbamazepine, phenytoin and phenobarbital
- an herbal remedy often used to treat depression called St. John's Wort
- other medicines used to treat multiple myeloma called melphalan and prednisone

How to use Velcade:

Velcade will be given to you by a healthcare professional. Velcade powder will first be mixed into a solution. This solution will then be given to you either

- by intravenous injection. This means it will be injected into a vein. The injection will take 3 to 5 seconds, or
- by subcutaneous injection. This means it will be given under the skin of either thigh or the abdomen. Your healthcare professional will decide the location of the injection. It will be rotated for each injection.

Frequency of treatment: How often you receive Velcade will depend on:

- the type of cancer you have,
- whether you have had a stem cell transplant,
- whether you have received previous treatment for your cancer, and
- how you respond to treatment.

Velcade is given in treatment cycles. This is a period of treatment that repeats on a regular schedule. A treatment cycle for Velcade can be between 3 weeks (21 days) and 6 weeks (42 days) long.

For patients with Multiple Myeloma that has not been previously treated:

If you can have a stem cell transplant:

- Treatment cycles are about 5 weeks long.
- You may receive between 3 and 6 treatment cycles.
- You will receive Velcade twice per week on days 1, 4, 8 and 11. This is followed by a rest period without treatment, which may be up to 20 days long.
- You will receive Velcade together with other medicines as initial treatment before starting the process for your stem cell transplant.

If you cannot have a stem cell transplant:

- Treatment cycles are 6 weeks long.
- You may receive 9 treatment cycles.
- For cycles 1 to 4: you will receive Velcade two times each week on days 1, 4, 8, 11, 22, 25, 29 and 32.
- For cycles 5 to 9: you will receive Velcade once a week on days 1, 8, 22 and 29.

For patients with Relapsed Multiple Myeloma and Relapsed or Refractory Mantle Cell Lymphoma:

- Treatment cycles are 3 weeks long. You may receive up to 8 eight cycles. For these cycles, you will receive Velcade twice per week on days 1, 4, 8 and 11.
- You may also receive maintenance treatment with Velcade. This means you may receive more than 8 cycles. For maintenance treatment, cycles are 4 weeks long. Velcade will be given once a week days 1, 8, 15 and 22.
- Your doctor may change your dose during the treatment and will decide the total number of cycles that you need. It will depend on your response to the treatment.

For patients with Mantle Cell Lymphoma that has not been treated previously:

- Treatment cycles are 3 weeks long.
- You may receive 6 to 8 cycles.
- Velcade will be given on days 1, 4, 8 and 11 of each cycle followed by a 10-day rest period (days 12-21) where there is no treatment.

Usual dose:

Usual adult dose: 1.3 mg/m². This means that the amount of Velcade you will receive depends on your height and weight.

Your healthcare professional may change your dose if you experience certain side effects.

Overdose:

As this medicine is being given by your healthcare professional, they will monitor you for side effects. Too much Velcade can affect your heart, blood pressure, heart rate and body temperature. It can also lead to death.

If you think you, or a person you are caring for, have taken too much Velcade, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed dose:

If you think that you have missed a dose of Velcade, tell your healthcare professional immediately.

What are possible side effects from using Velcade?

These are not all the possible side effects you may have when taking Velcade. If you experience any side effects not listed here, tell your healthcare professional.

- Blurred vision
- Abdominal pain
- Heartburn
- Stomach ulcers
- General ill feeling
- Flu-like symptoms
- Tiredness
- Feeling of weakness
- Swelling of the arms, legs or face
- Shivering
- Weight loss
- Joint or muscle stiffness
- Muscle or bone pain
- Back pain
- Dizziness
- Difficulty sleeping
- Anxiety or depression (feeling down)
- Shortness of breath
- Cough
- Itching
- Hives
- Redness
- Pain at the injection site
- Sudden fall of blood pressure on standing which may lead dizziness, light-headedness and fainting

Serious side effects and what to do about them		
Symptom / effect	Talk with your healthcare professional	
	Only if severe	In all cases
Common		
Fever		✓
Chest and other infections including shingles: fever, chills, nausea, vomiting, diarrhea, generally feeling unwell, painful skin rash of fluid-filled blisters		✓
Diarrhea	✓	
Vomiting	✓	
Dehydration: dry mouth, excessive thirst, dark yellow urine		✓
Nausea	✓	
Dyspnea: Difficulty breathing/breathlessness	✓	
Parasthesia: altered sensation or feeling of burning or pins and needles in hands or feet	✓	
Peripheral neuropathy (damage to nerves): pain and altered sensation, weakness, numbness usually in the hands and feet		✓
Hemorrhage (bleeding): bleeding from gums or other sites, abnormal bruising		✓
Tiredness/lethargy	✓	
Joint pain and muscle cramps	✓	
Headache	✓	
Hypotension (low blood pressure): dizziness or fainting		✓
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		✓
Low blood cell counts including: Anemia (low red blood cells): fatigue, loss of energy, pale skin, shortness of breath, weakness Thrombocytopenia (low blood platelets): bruising or bleeding, fatigue, weakness Leukopenia / neutropenia / lymphopenia (low white blood cells): infections, fatigue, fever, aches, pains, flu-like symptoms		✓
Uncommon		
Facial Edema: Swelling of face or neck		✓
Edema: Swelling of ankles	✓	

Serious side effects and what to do about them		
Symptom / effect	Talk with your healthcare professional	
	Only if severe	In all cases
Heart problems including: Heart Failure (heart does not pump blood as well as it should): breathlessness, difficulty breathing when lying down, swelling of the feet, ankles or legs, weakness/tiredness Arrhythmia (abnormal heart rhythm): Chest palpitations; rapid, slow or irregular heartbeat, abnormal electrical signal from an electrocardiogram (ECG) reading		✓
Angina (not enough oxygen to the heart muscle): chest pain, discomfort in the shoulder, arm, back, throat jaw or teeth	✓	
Loss of appetite	✓	
Severe abdominal pain with or without bleeding		✓
Constipation	✓	
Jaundice: Yellowing of skin or whites of eyes		✓
Skin rash		✓
Stroke (bleeding or blood clot in the brain): difficulty moving limbs, walking or speaking, sudden numbness, weakness or tingling of the face, arm, or leg, particularly on one side of the body, sudden headache, blurry vision, difficulty swallowing or speaking, or lethargy, dizziness, fainting, vomiting, trouble understanding, trouble with walking and loss of balance		✓
Confusion		✓
Seizure (fits): uncontrollable shaking with or without loss of consciousness		✓
Kidney Damage: loss of control or inability to pass urine		✓
Muscle weakness	✓	
Nervous system disorders: new onset or worsening neurological signs or symptoms such as confusion or problems thinking, loss of balance, blurred vision or loss of vision, decreased strength or weakness in an arm or leg or change in the way of walking or talking (these may be signs of a serious brain infections and your doctor may suggest further testing and follow-up)		✓
Pericarditis (inflammation of the lining around the heart): chest pain, difficulty breathing when lying down, swelling of the feet, ankles or legs, weakness/ tiredness, cough, fever, heart palpitations		✓

Serious side effects and what to do about them		
Symptom / effect	Talk with your healthcare professional	
	Only if severe	In all cases
Anaphylactic (allergic) reaction: difficulty breathing, chest pain or chest tightness, and/or feeling dizzy/faint, severe itching of the skin or raised lumps on the skin, swelling of the face, lips, tongue and /or throat, which may cause difficulty in swallowing		✓
Sepsis or Septic Shock (infection in the bloodstream): fever, increased heart rate or breathing, confusion		✓
Tumour Lysis Syndrome (sudden, rapid death of cancer cells due to the treatment): nausea, shortness of breath, irregular heartbeat, heart rhythm disturbances, lack of urination, clouding of urine, muscle spasms or twitching, tiredness and/or joint pain, severe muscle weakness, and seizures		✓
Pulmonary Hypertension (high blood pressure in the lungs): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling of ankles and legs, bluish colour to lips and skin, heart palpitations		✓
Rare		
Blepharitis (inflammation of the eyelid): red and swollen eyelids	✓	
Chalazion: red cyst (bump) on the eyelid	✓	
Posterior reversible encephalopathy syndrome (PRES): seizure, high blood pressure, headache, lethargy, confusion, speech and vision loss		✓
Autonomic Neuropathy (damage to nerves that control automatic body functions): feeling dizzy upon sitting up or standing up, diarrhea, constipation, fever, urination problems, sweating too much or too little		✓
Acute Diffuse Infiltrative Pulmonary Disease (inflamed or scarred lung): cough, difficulty breathing, breathlessness		✓
Very Rare		
Thrombotic Microangiopathy (blood clot in very small blood vessels): bleeding, bruising, and kidney injury (decreased urine, swollen legs, high blood pressure)		✓

Serious side effects and what to do about them		
Symptom / effect	Talk with your healthcare professional	
	Only if severe	In all cases
Progressive multifocal Leukoencephalopathy (PML) (a rare brain infection): progressive weakness on one side of the body, clumsiness of limbs, disturbance of vision, changes in thinking, memory and orientation, confusion, personality changes		✓
Guillain-Barré Syndrome / demyelinating polyneuropathy (when inflammation attacks peripheral nerves): numbness, weakness, paralysis, difficulty breathing, chewing or swallowing, changes in blood pressure or heartrate		✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Your healthcare professional will store Velcade at 15 to 30°C. They will keep the vial in its outer carton to protect it from light and will be sure to use it before its expiry date. If the powder is mixed into a solution, the solution will be stored for no more than 8 hours at 25°C in the original vial or a syringe prior to administration, with a maximum of 8 hours in the syringe.

If you want more information about Velcade:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug->

products/drug-product-database.html; the manufacturer's website
www.janssen.com/canada, or by calling 1-800-567-3331 or 1-800-387-8781.

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