READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

Pr MVASI®

Pronounced *em vah' see*

bevacizumab

Read this carefully before you start taking **MVASI** 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 **MVASI**.

MVASI is a biosimilar biologic drug (biosimilar) to the reference biologic drug AVASTIN®. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.

Serious Warnings and Precautions

- **Eye Disorders**

  MVASI was not developed to be injected in the eye and should be used as authorized. Side effects affecting the eye and the body as a whole were seen in some patients who had bevacizumab injected in their eye(s).

- **Gastrointestinal Perforations**

  MVASI treatment can cause gastrointestinal perforation, (hole in the stomach or bowel) which can be fatal.

  MVASI treatment should be stopped if this happens. Gastrointestinal perforation can happen at any time during treatment: symptoms include abdominal pain, constipation, and vomiting.

- **Wound Healing Complications**

  MVASI treatment can cause wound dehiscence (wounds opening and not healing), which can be fatal. MVASI treatment should be stopped if this happens and for one month after having surgery or until the wound is fully healed. MVASI should be stopped at least 28 days before elective surgery.

- **Hemorrhage**

  Treatment with MVASI can result in serious or fatal bleeding, including coughing up blood, bleeding in the stomach, vomiting of blood, bleeding in the brain, nosebleeds, and vaginal bleeding. These events occurred up to 5 times more often in people who received bevacizumab compared to patients who received only chemotherapy. People who have recently coughed up blood (greater than or equal to a half teaspoon of red blood) or have serious bleeding should not receive MVASI. Treatment with MVASI should be permanently stopped if serious bleeding occurs (ie, requiring medical attention).

What is MVASI used for?

Metastatic Colorectal Cancer: MVASI is used in combination with a specific type of chemotherapy (intravenous 5-fluorouracil [5-FU]-based chemotherapy) for treatment of patients diagnosed with metastatic colorectal cancer for the first time. Metastatic colorectal cancer is cancer of the colon or rectum that has spread to other organs in the body.

Metastatic Lung Cancer: MVASI is used in combination with a specific type of chemotherapy (carboplatin and paclitaxel) for the treatment of people diagnosed with metastatic non-small cell lung cancer. Metastatic non-small cell lung cancer is cancer of the lungs that has spread to other organs in the body.

Recurrent Platinum-Sensitive Ovarian Cancer: MVASI is used in combination with a specific type of chemotherapy (carboplatin and gemcitabine) for the treatment of people diagnosed with recurrent, platinum-sensitive, epithelial ovarian, fallopian tube, or primary peritoneal cancer that comes back at least 6 months after the last time the patient responded to a chemotherapy regimen containing a platinum agent. Epithelial ovarian cancer is cancer that develops on the surface of the ovary. Fallopian tube cancer is cancer that forms in a woman's fallopian tubes, the small ducts that link a woman's ovaries to her uterus. Primary peritoneal cancer is cancer of the tissue that lines the abdominal wall and covers organs in the abdomen.

Recurrent Platinum-Resistant Ovarian Cancer: MVASI is used in combination with a specific type of chemotherapy (paclitaxel, topotecan, or pegylated liposomal doxorubicin) for the treatment of people diagnosed with recurrent, platinum-resistant, epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than two prior chemotherapy regimens. Recurrent platinum-resistant ovarian cancer is the type of cancer that progresses within 6 months after the last time the patient responded to a chemotherapy regimen containing a platinum agent.

Recurrent Glioblastoma: MVASI is used in combination with lomustine (a specific type of chemotherapy) for the treatment of patients with a particular type of brain cancer called glioblastoma in which the cancer reoccurred after a previous treatment.

How does MVASI work?

MVASI is not chemotherapy but is given in combination with a specific type of chemotherapy. MVASI is a monoclonal antibody. While chemotherapy attacks the tumour directly, MVASI attacks the blood vessels that surround the tumour.

In order to grow and spread, tumours need a constant supply of oxygen and other nutrients. Tumours get this supply by creating their own network of blood vessels. This process is called angiogenesis (an´-gee-o-jen´-i-sis). MVASI works by blocking angiogenesis. By preventing the growth of new blood vessels, MVASI helps starve the tumour of oxygen and other nutrients. This makes it hard for the tumour to grow.

What are the ingredients in MVASI?

- The medicinal ingredient is called bevacizumab.
- The non-medicinal ingredients are (in alphabetical order): α,α-trehalose dihydrate, polysorbate 20, sodium phosphate and water for injection.

MVASI comes in the following dosage forms:

MVASI is available as single use vials in the presentations listed below:

- 100 mg/4 mL (25 mg/mL)
- 400 mg/16 mL (25 mg/mL)

Do not use MVASI if:

MVASI should not be used by people who are allergic to it or any of its ingredients or by people whose cancer has spread to their central nervous system (to their brain or spine). MVASI should not be taken for at least 28 days following surgery.

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

- have high blood pressure
- plan to have surgery or have had surgery in the last 28 days
- have ever had a heart attack or stroke
- are pregnant or plan to become pregnant
- are breast feeding
- have any allergies to this drug or its ingredients
- have any illnesses or diseases affecting your kidneys
- have heart failure or weakened heart muscles
- have ever coughed up blood or observed abnormal vaginal bleeding
- are diabetic.

Other warnings you should know about:

MVASI should not be used during pregnancy as it may cause harm to your unborn baby. Therefore, you should use effective methods of contraception while taking MVASI and for at least 6 months after your last dose of MVASI. If you become pregnant during treatment with MVASI, tell your doctor immediately.

MVASI may affect the hormonal balance of women and their ability to get pregnant as a result of ovarian failure. If you are a woman of reproductive potential, talk to your doctor before starting treatment with MVASI.

If you develop headache, vision problems, dizziness, or change in mental status (for example, confusion) contact your doctor immediately.

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 MVASI:

- Drugs that may interact with MVASI include: irinotecan and sunitinib malate. Your doctor may adjust the dose of irinotecan if you have side effects known to be related to it. The safety and effectiveness of MVASI in combination with sunitinib malate has not been established, therefore this combination is not recommended.
- Tell your doctor if you are using platinum- or taxane-based therapies for lung cancer. These therapies in combination with MVASI may increase the risk of severe side effects.

- The interaction of MVASI in combination with EGFR monoclonal antibodies has not been studied, therefore this combination is not recommended.

How to take MVASI?

Dosage and frequency of administration

The dose of MVASI needed depends on your body weight and the kind of cancer to be treated. If you have:

- Metastatic Colorectal Cancer, you will receive 5 mg/kg of your body weight once every 2 weeks.
- Metastatic Lung Cancer, you will receive 15 mg/kg of your body weight once every 3 weeks.
- Ovarian Cancer (Platinum-sensitive recurrent disease), you will receive 15 mg/kg of your body weight once every 3 weeks.
- Ovarian Cancer (Platinum-resistant recurrent disease), you will receive 10 mg/kg or 15 mg/kg of your body weight once every 2 or 3 weeks.
- Recurrent Glioblastoma, you will receive 10 mg/kg of your body weight once every 2 weeks.

Your doctor will prescribe a dose of MVASI that is right for you.

A doctor or nurse will give you a diluted MVASI solution by intravenous infusion (a drip in your vein). The first infusion will be given to you over 90 minutes. If this is well-tolerated the second infusion may be given over 60 minutes. Later infusions may be given to you over 30 minutes. The number of infusions that you receive will depend on how you are responding to treatment; you should continue to receive this medicine until MVASI fails to stop your tumour growing. Your doctor will discuss this with you.

Usual Dose:

Metastatic Colorectal Cancer:

- The usual dose of MVASI is based on your weight in kg (5 mg/kg) and it is given once every 14 days for as long as your physician recommends therapy.

Metastatic Lung Cancer:

- The usual dose of MVASI is based on your weight in kg (15 mg/kg) and on the specific type of chemotherapy given along with the MVASI. MVASI is given once every 3 weeks for as long as your physician recommends therapy.

Ovarian Cancer (Platinum-sensitive recurrent disease):

- The usual dose of MVASI is based on your weight in kg (15 mg/kg). MVASI is given once every 3 weeks for as long as your physician recommends therapy. Your doctor will prescribe a dose and schedule of MVASI that is right for you, based on if and what type of chemotherapy you are also receiving.

Ovarian Cancer (Platinum-resistant recurrent disease):

- The usual dose of MVASI is based on your weight in kg (10 mg/kg or 15 mg/kg). MVASI is given once every 2 weeks or 3 weeks for as long as your physician recommends therapy. Your doctor will prescribe a dose and schedule of MVASI that is right for you, based on if and what type of chemotherapy you are also receiving.

Recurrent Glioblastoma:

- The usual dose of MVASI is based on your weight in kg (10 mg/kg). MVASI is given once every 2 weeks in combination with lomustine every 6 weeks for as long as your physician recommends therapy. The dose of lomustine in the first treatment is 90 mg per square metre of your body surface area (mg/m^2), up to a maximum dose of 160 mg. It can be increased to 110 mg/m^2, up to a maximum 200 mg, from the second treatment onwards. The increase in dose of lomustine after the first treatment will be determined by your doctor based on your blood work.

Overdose:

If you think you have taken too much MVASI, particularly accidental oral ingestion, contact your healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

In addition to the possible side effects listed below, an overdose may cause a severe headache.

Missed Dose:

If you miss a dose of MVASI, your doctor will decide when you should receive your next dose.

What are possible side effects from using MVASI?

These are not all the possible side effects you may feel when taking MVASI. If you experience any side effects not listed here, contact your healthcare professional.

Very Common (more than 1 in 10 patients):

- High blood pressure
- Diarrhea
- Vomiting
- Abdominal pain
- Constipation
- Nausea
- Lack of energy or strength
- Loss of appetite
- Pain (including joint pain)
- Bleeding (from the nose or rectum)
- Sores in the mouth
- Shortness of breath
- Runny nose
- Dry, scaling skin or changes in skin colour
- Changes in the sense of taste
- Eye problems (for example: excessive tearing, blurred vision, an experience of discomfort or pain to the eyes due to light exposure)

- A decrease in certain white blood cells in the blood that help fight off infection
- Decrease in the number of red blood cells (anemia)
- Difficulty in sleeping
- Fever, chills or excessive sweating
- Headache
- Abnormal urine test (protein in the urine)
- Tingling sensation or numbness in toes and fingers
- Bronchitis (an inflammation of the main air passages to the lungs)
- Bruising
- Change in moods
- Infections (mouth, throat, sinus, lungs or urine infections)
- Excess of sugar in the blood
- Weight loss
- Widening of the blood vessels
- Low levels of sodium and magnesium in the blood
- Coughing
- Tiredness

Common side effects (less than 1 in 10 patients but more than 1 in 100 patients):

- Pain (including muscle pain, chest pain, heart pain (angina), back pain, and pain in the pelvis and anal regions)
- Stroke/heart attack
- Blood clots
- Perforation of the gut (hole in the stomach or bowel)
- Altered voice such as hoarseness
- Swelling and numbness of the hand and feet
- Urinary (bladder or kidney) infection
- Infections of the skin or deeper layers under the skin
- Fistula (abnormal tube like connection between internal parts of the body that are not normally connected) such as between the stomach and intestines (gastrointestinal fistula), in patients with metastatic colorectal cancer, and recurrent ovarian cancer and between the vagina and the gut in patients with cervical cancer (unauthorized use)
- Allergic reactions
- Nephrotic syndrome (a type of kidney disorder)

Uncommon side effects (less than 1 in 100 patients but more than 1 in 1000 patients):

- Non-gastrointestinal perforations and fistulae (abnormal holes or tubes in areas of the body other than the gastrointestinal tract)
- Posterior Reversible Encephalopathy Syndrome (PRES) a syndrome characterized by headache, confusion, seizures and visual loss

Rare (less than 1 in 1000 patients but more than 1 in 10,000 patients):

- Tracheoesophageal fistula (abnormal tube like connection between internal parts of the body that are not normally connected) such as between the trachea (or windpipe) and esophagus (tube connecting the mouth to the stomach)
- Severe bacterial infection of the skin and soft tissue (necrotizing fasciitis)
- Bleeding (in the brain)

Frequency unknown:

- Ulcers in the stomach and bowel
- Jaw bone damage resulting from poor blood supply to the jaw bone
- Perforation in the gallbladder (hole in the digestive organ that stores bile)

If your blood pressure increases while you are taking MVASI, it is important to contact your doctor.

Changes in your blood and urine tests done by your doctor may occur while you are receiving MVASI. These changes may include a lower white cell count, and protein in the urine. Your doctor will discuss these results with you.

Elderly patients (65 years or older) have a greater risk of developing the following side effects: blood clots (that may lead to stroke or heart attack), a decrease in certain white blood cells and platelets, protein in the urine, diarrhea and fatigue.

Outside of the authorized use of MVASI for cancer treatment, the following side effects may occur when MVASI is injected directly into the eye (unauthorized use):

- Infection or inflammation of the eye globe, which may lead to permanent blindness
- Redness of the eye, small particles or spots in your vision (floaters), eye pain, which may lead to permanent blindness
- Seeing flashes of light with floaters, progressing to a loss of some of your vision
- Increased eye pressure
- Bleeding in the eye
- Surgery of the eye lens due to cataract
- Other serious side effects affecting other organs, which may be severe and lead to hospitalization, eg, heart attack, stroke, and high blood pressure.

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional in all cases**	**Stop taking drug and get immediate medical help**
VERY COMMON (more than 1 in 10 patients)		
High blood pressure	✓	
• You may not experience any symptoms, but possible symptoms associated with high blood pressure are: headache, blurred vision, fatigue, irregular, fast, hard heartbeats		
Bleeding from the nose that lasts more than 10-15 minutes and cannot be stopped		✓
Diarrhea	✓	
Vomiting	✓	
Constipation	✓	
Bleeding from the rectum or stomach	✓	
• Symptoms include fresh blood in stools and/or dark stools		
Decreased number of white blood cells	✓	
• Symptoms could include fever, sore throat, infection		
Decreased number of red blood cells in the blood that carry oxygen	✓	
• Symptoms could include feeling of weakness or fatigue in general or during exercise, poor concentration		
Pain (chest pain, back pain, abdominal pain, muscle pain, joint pain)	✓	
Low blood pressure	✓	
• You may not experience any symptoms, but possible symptoms associated with low blood pressure are: lightheadedness, dizziness, fainting		
Dilation (widening) of the blood vessels	✓	
• Symptoms may include low blood pressure, dizziness, flushing		
Bronchitis (an inflammation of the main air passages to the lungs)	✓	
Excess of sugar in the blood	✓	
• Symptoms may include frequent hunger, frequent thirst, frequent urination		
Infections (mouth, throat, sinus, lungs or urine infections)	✓	

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional in all cases**	**Stop taking drug and get immediate medical help**
Weakened heart muscle/loss of the heart's pumping ability • Symptoms may include shortness of breath, fatigue, persistent coughing or wheezing, increased heart rate, swelling in the feet or ankles	✓	
Low levels of sodium and magnesium in the blood	✓	
Coughing	✓	
COMMON (less than 1 in 10 patients but more than 1 in 100 patients)		
Perforation of the gut (leakage of the bowel) • Symptoms include: sudden onset of abdominal pain, abdominal tenderness with vomiting, high fever		✓
Allergic reactions • Symptoms include difficulty in breathing, chest pain, redness or flushing of the skin, rash, shivering, nausea, vomiting	✓	
Blood clots • In the deep veins of the leg, symptoms include: pain, swelling, warm to the touch, and tenderness of the leg • In the lung, symptoms include: shortness of breath, chest pain, light headedness	✓	
Stroke or heart attack • Symptoms of stroke include: sudden loss of speech or numbness of part or all of the body, loss of vision or blurred vision, unexplained dizziness and/or sudden falls. • Symptoms of a heart attack include: chest pain with spreading to the left arm, jaw and/or back, shortness of breath		✓
Pain • in the pelvis and anal regions	✓	
Fistula • Abnormal tube-like connection between internal organs and skin or other tissues that are not normally connected, including connections between the vagina and the gut in patients with cervical cancer (unauthorized use)		✓
Nephrotic syndrome (a type of kidney disorder) • Symptoms include swelling in the face, arms, legs, belly area, foamy appearance of urine and poor appetite	✓	

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional in all cases**	**Stop taking drug and get immediate medical help**
UNCOMMON (less than 1 in 100 patients but more than 1 in 1000 patients)		
Non-gastrointestinal perforations and fistulae • Depending on the organs involved the symptoms could be as follows: leakage of urine, abnormal and bad odor in the genital area, abdominal pain, vomiting, fever, gradually increasing/worsening of shortness of breath (dyspnea), cough, chest pain, yellowish discoloration of the skin etc.	✓	✓
Posterior Reversible Encephalopathy Syndrome (PRES) • Symptoms include headache, confusion, seizures and visual loss		✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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 (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) 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:

Store vials in a refrigerator at 2ºC to 8ºC. Do not freeze. Do not shake.

Keep vial in the outer carton in order to protect from light.

Keep out of the reach and sight of children.

If you want more information about MVASI:

- 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 (http://hc-sc.gc.ca/index-eng.php); the manufacturer's website www.amgen.ca, or by calling 1-866-502-6436.

This leaflet was prepared by Amgen Canada Inc.

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