

PRODUCT MONOGRAPH

Pr AVASTIN[®]

bevacizumab for injection

100 mg and 400 mg vials (25 mg/mL solution for injection)

Antineoplastic

Hoffmann-La Roche Limited
7070 Mississauga Road
Mississauga, Ontario
L5N 5M8

www.rochecanada.com

Submission Control No: 207259

Date of Approval: June 6, 2018

AVASTIN[®] is a registered trade-mark of Genentech, Inc., used under license.
© Copyright 2005-2018 by Hoffmann-La Roche Limited.

Table of Contents

PART III: CONSUMER INFORMATION..... 3

PART III: CONSUMER INFORMATIONPr **AVASTIN**[®]

bevacizumab

Metastatic Colorectal Cancer, Metastatic Lung Cancer, Recurrent Glioblastoma, and Recurrent Ovarian Cancer that previously responded to a platinum-based treatment

This leaflet is part III of a three-part "Product Monograph" published when AVASTIN (pronounced ah-vah'-stin) was authorized for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about AVASTIN. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATIONWhat the medication is used for:

Metastatic Colorectal Cancer: AVASTIN is used in combination with a specific type of chemotherapy (intravenous 5-fluorouracil [5-FU]-based chemotherapy) for treatment of people 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: AVASTIN 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: AVASTIN 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: AVASTIN 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: AVASTIN 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.

What it does:

AVASTIN is not chemotherapy but is given in combination with a specific type of chemotherapy. AVASTIN is a monoclonal antibody. While chemotherapy attacks the tumour directly, AVASTIN 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). AVASTIN works by blocking angiogenesis. By preventing the growth of new blood vessels, AVASTIN helps starve the tumour of oxygen and other nutrients. This makes it hard for the tumour to grow.

When it should not be used:

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

days following surgery.

What the medicinal ingredient is:

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.

What dosage forms it comes in:

AVASTIN is given intravenously (through a needle placed in a vein in the arm, hand, or through a central line).

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Eye disorders

AVASTIN 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 AVASTIN injected in their eye(s).

Gastrointestinal Perforations

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

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

Hemorrhage

Treatment with AVASTIN 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 AVASTIN 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 AVASTIN. Treatment with AVASTIN should be permanently stopped if serious bleeding occurs (i.e. requiring medical attention).

BEFORE you use AVASTIN talk to your doctor or pharmacist 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.

AVASTIN 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 AVASTIN and for at least 6 months after your last dose of AVASTIN. If you become pregnant during treatment with AVASTIN, tell your doctor immediately.

AVASTIN 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 AVASTIN.

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

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with AVASTIN 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 AVASTIN 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. These therapies in combination with AVASTIN may increase the risk of severe side effects.

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

PROPER USE OF THIS MEDICATION

Usual dose:

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

Ovarian Cancer (Platinum-sensitive recurrent disease): The usual dose of AVASTIN is based on your weight in kg (15 mg/kg). AVASTIN is given once every 3 weeks for as long as your physician recommends therapy.

Ovarian Cancer (Platinum-resistant recurrent disease): The usual dose of AVASTIN is based on your weight in kg (10 mg/kg or 15 mg/kg). AVASTIN 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 AVASTIN that is right for you, based on if and what type of chemotherapy you are also receiving.

Recurrent Glioblastoma: The usual dose of AVASTIN is based on your weight in kg (10 mg/kg). AVASTIN 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 dose of lomustine after the first treatment will be determined by your doctor based on your blood work.

The first time AVASTIN is given, it will take about 90 minutes. Once your doctor has made sure that you have no problems with the AVASTIN infusions, (i.e. after the first or second infusion), subsequent infusions may require less time, usually about 30 or 60 minutes.

Overdose:

In case of drug overdose or suspected drug overdose, particularly accidental oral ingestion, contact a healthcare practitioner (e.g. doctor), hospital emergency department, or regional poison control centre, 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 AVASTIN, your doctor will decide when you should receive your next dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medications, AVASTIN can cause some unwanted side effects. The following side effects were seen in clinical trials when AVASTIN in combination with chemotherapy or AVASTIN alone was given to patients:

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 (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 (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 AVASTIN, it is important to contact your doctor.

Changes in your blood and urine tests done by your doctor may occur while you are receiving AVASTIN. 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 AVASTIN for cancer treatment, the following side effects may occur when AVASTIN 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 hospitalisation, e.g. heart attack, stroke, and high blood pressure

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist in all cases	Seek emergency medical treatment
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	✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist in all cases	Seek emergency medical treatment
	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)	✓	
	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	✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist in all cases	Seek emergency medical treatment
	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.	✓	
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 (dyspnoea), cough, chest pain, yellowish discoloration of the skin etc.	✓	✓
	Posterior Reversible Encephalopathy Syndrome (PRES) -Symptoms include headache, confusion, seizures and visual loss.		✓

This is not a complete list of side effects. For any unexpected effects while taking AVASTIN, contact your doctor or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: **Canada Vigilance Program
Health Canada
Postal Locator 1908C
Ottawa, ON KIA OK9**

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: www.rochecanada.com or by contacting the sponsor, Hoffmann-La Roche Limited, at 1-888-762-4388.

This leaflet was prepared by Hoffmann-La Roche Limited.

Last revised: May 31, 2018

©Copyright 2005-2018 by Hoffmann-La Roche Limited

AVASTIN[®] is a registered trade-mark of Genentech, Inc., used under license



Hoffmann-La Roche Limited
Mississauga, ON L5N 5M8