

## PATIENT MEDICATION INFORMATION

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

<sup>Pr</sup>AYBINTIO®

#### Bevacizumab for injection

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

**AYBINTIO** is a biosimilar biologic drug (biosimilar) to the reference biologic drug <sup>Pr</sup>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

AYBINTIO should not be injected in the eye. Side effects were seen in the eye and body as a whole in some patients who had AYBINTIO injected in the eye.

##### Hole in the stomach or bowel

At any time during treatment, AYBINTIO may cause a hole in the stomach or bowel which can be deadly. Treatment should be stopped if this happens. Side effects include stomach pain, constipation, and vomiting.

##### Wound healing complications

AYBINTIO may cause wounds to open and not heal, which can be deadly. AYBINTIO treatment should be stopped if this happens and for one month after having surgery or until the wound is fully healed. AYBINTIO should be stopped at least 28 days before elective surgery.

##### Bleeding

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

#### What is AYBINTIO used for?

Metastatic Colorectal Cancer: AYBINTIO 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:** AYBINTIO 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:** AYBINTIO 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:** AYBINTIO 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:** AYBINTIO 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 AYBINTIO work?**

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

### **What are the ingredients in AYBINTIO?**

The medicinal ingredient is called bevacizumab.

The non-medicinal ingredients are (in alphabetical order): Acetic acid, polysorbate 20, sodium acetate trihydrate, trehalose dihydrate, water for injection.

### **AYBINTIO comes in the following dosage forms:**

AYBINTIO 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 AYBINTIO if:**

- you are allergic to bevacizumab or any of its ingredients in Avastin; your cancer has spread to your brain or spine. AYBINTIO 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 AYBINTIO. Talk about any health conditions or problems you may have, including if you:**

- have high blood pressure;
- are pregnant or plan to become pregnant;
- are breast feeding;
- have any allergies to this drug or its ingredients;
- plan to have surgery or have had surgery in the last 28 days;
- 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:**

- **Children and adolescents:** AYBINTIO should not be given to children or adolescents. This is because the effects of AYBINTIO in people younger than 18 years of age are not known.

**Females of childbearing potential:** AYBINTIO may cause fertility problems. AYBINTIO 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 AYBINTIO. AYBINTIO 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 AYBINTIO and for at least 6 months after your last dose of AYBINTIO. If you become pregnant during treatment with AYBINTIO, tell your doctor immediately.

**Driving and using machines:** It is not known whether AYBINTIO affects your ability to drive or use tools or machines.

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 AYBINTIO:**

- **irinotecan:** Your doctor may adjust the dose of irinotecan if you have side effects known to be related to it.

**sunitinib malate:** the safety and efficacy of AYBINTIO in combination with sunitinib malate has not been established, therefore this combination is not recommended.

**platinum- or taxane-based therapies for lung:** These therapies in combination with AYBINTIO may increase the risk of severe side effects.

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

### **How to take AYBINTIO:**

AYBINTIO will be given to you by a healthcare professional in a healthcare setting. Do not use this medication if it looks cloudy or is leaking.

### **Usual dose:**

#### Metastatic Colorectal Cancer

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

#### Ovarian Cancer (Platinum-sensitive recurrent disease)

The usual dose of AYBINTIO is based on your weight in kg (15 mg/kg). AYBINTIO is given once every 3 weeks for as long as your physician recommends therapy.

#### Ovarian Cancer (Platinum-resistant recurrent disease)

The usual dose of AYBINTIO is based on your weight in kg (10 mg/kg or 15 mg/kg). AYBINTIO 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 AYBINTIO that is right for you, based on if and what type of chemotherapy you are also receiving.

#### Recurrent Glioblastoma

The usual dose of AYBINTIO is based on your weight in kg (10 mg/kg). AYBINTIO 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 ( $\text{mg}/\text{m}^2$ ), up to a maximum dose of 160 mg. It can be increased to 110  $\text{mg}/\text{m}^2$ , 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 AYBINTIO is given, it will take about 90 minutes. Once your doctor has made sure that you have no problems with the AYBINTIO infusions, (i.e. after the first or second infusion), subsequent infusions may require less time, usually about 30 or 60 minutes.

### **Overdose:**

If you think you, or a person you are caring for, have taken too much AYBINTIO, contact a 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 AYBINTIO, your doctor will decide when you should receive your next dose.

### **What are possible side effects from using AYBINTIO?**

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

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

Very Common (more effect more than 1 in 10 patients):

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- Lack of energy or strength
- Loss of appetite
- Sores in the mouth
- Runny nose
- Dry, scaling skin or changes in skin colour
- Changes in the sense of taste
- Difficulty in sleeping
- Chills or excessive sweating
- Abnormal urine test (protein in the urine)
- Tingling sensation or numbness in toes and fingers
- Bruising
- Change in moods
- Weight loss
- Tiredness

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

- Heart pain (angina)
- Altered voice such as hoarseness
- Swelling and numbness of the hand and feet

Frequency unknown:

- Ulcers in the stomach and bowel

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

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

<b>Serious side effects and what to do about them</b>			
<b>Symptom / effect</b>	<b>Talk to your healthcare professional</b>		<b>Stop taking drug and get immediate medical help</b>
	<b>Only if severe</b>	<b>In all cases</b>	
<b>VERY COMMON</b>			
High blood pressure <ul style="list-style-type: none"> <li>• You may not experience any symptoms, but possible symptoms associated with high blood pressure are: headache, blurred vision, fatigue, irregular, fast, hard heartbeats.</li> </ul>		✓	
Bleeding from the nose that lasts more than 10-15 minutes and cannot be stopped.		✓	✓
Diarrhea		✓	
Vomiting		✓	
Constipation		✓	
Bleeding from the rectum or stomach <ul style="list-style-type: none"> <li>• Symptoms include fresh blood in stools and/or dark stools</li> </ul>		✓	
Decreased number of white blood cells <ul style="list-style-type: none"> <li>• Symptoms could include fever, sore throat, infection</li> </ul>		✓	
Decreased number of red blood cells in the blood that carry oxygen <ul style="list-style-type: none"> <li>• Symptoms could include feeling of weakness or fatigue in general or during exercise, poor concentration</li> </ul>		✓	
Pain (chest pain, back pain, abdominal pain, muscle pain, joint pain)		✓	
Low blood pressure <ul style="list-style-type: none"> <li>• You may not experience any symptoms, but possible</li> </ul>		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
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symptoms associated with low blood pressure are: lightheadedness, dizziness, fainting.			
Dilation (widening) of the blood vessels <ul style="list-style-type: none"> <li>Symptoms may include low blood pressure, dizziness, flushing</li> </ul>		✓	
Bronchitis (an inflammation of the main air passages to the lungs)		✓	
Excess of sugar in the blood <ul style="list-style-type: none"> <li>Symptoms may include frequent hunger, frequent thirst, frequent urination</li> </ul>		✓	
Infections (mouth, throat, sinus, lungs or urine infections)		✓	
Weakened heart muscle/loss of the heart's pumping ability <ul style="list-style-type: none"> <li>Symptoms may include shortness of breath, fatigue, persistent coughing or wheezing, increased heart rate, swelling in the feet or ankles</li> </ul>		✓	✓
Eye problems <ul style="list-style-type: none"> <li>for example: excessive tearing, blurred vision, an experience of discomfort or pain to the eyes due to light exposure</li> </ul>		✓	
Low levels of sodium and magnesium in the blood		✓	
Coughing		✓	
<b>COMMON</b>			
Perforation of the gut (leakage of the bowel) <ul style="list-style-type: none"> <li>Symptoms include: sudden onset of abdominal pain, abdominal tenderness with vomiting, high fever.</li> </ul>		✓	✓
Allergic reactions <ul style="list-style-type: none"> <li>Symptoms include difficulty in breathing, chest pain, redness or flushing of the skin, rash, shivering, nausea, vomiting</li> </ul>		✓	✓
Urinary (bladder or kidney) infection		✓	✓
Infections of the skin or deeper layers under the skin		✓	✓
Blood clots <ul style="list-style-type: none"> <li>In the deep veins of the leg,</li> </ul>		✓	✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
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symptoms include: pain, swelling, warm to the touch, and tenderness of the leg. <ul style="list-style-type: none"> <li>In the lung, symptoms include: shortness of breath, chest pain, light headedness</li> </ul>			
Stroke or heart attack <ul style="list-style-type: none"> <li>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.</li> <li>Symptoms of a heart attack include: chest pain with spreading to the left arm, jaw and/or back, shortness of breath.</li> </ul>		✓	✓
Hemorrhage <ul style="list-style-type: none"> <li>gastrointestinal bleeding, significant blood in vomit, bleeding from rectum or stomach (fresh blood in stools or dark stool), bleeding from the nose that lasts more than 10-15 minutes and cannot be stopped, spitting of blood</li> </ul>		✓	✓
Wounds opening and not healing <ul style="list-style-type: none"> <li>the skin near a surgical area can appear fully or partially open</li> </ul>		✓	✓
Pain- in the pelvis and anal regions		✓	
Fistula <ul style="list-style-type: none"> <li>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)</li> </ul>		✓	✓
Nephrotic syndrome (a type of kidney disorder) <ul style="list-style-type: none"> <li>Symptoms include swelling in the face, arms, legs, belly area, foamy appearance of urine and poor appetite.</li> </ul>		✓	✓
<b>UNCOMMON</b>			
Non-gastrointestinal perforations and fistulae		✓	✓



Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<ul style="list-style-type: none"> <li>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.</li> </ul>			
Posterior Reversible Encephalopathy Syndrome (PRES) <ul style="list-style-type: none"> <li>Symptoms include headache, confusion, seizures and visual loss.</li> </ul>		✓	✓
<b>RARE</b>			
Tracheoesophageal fistula <ul style="list-style-type: none"> <li>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)</li> </ul>		✓	✓
Severe bacterial infection of the skin and soft tissue <ul style="list-style-type: none"> <li>necrotizing fasciitis</li> </ul>		✓	✓
Bleeding: in the brain		✓	✓
<b>FREQUENCY UNKNOWN</b>			
Jaw bone damage resulting from poor blood supply to the jaw bone		✓	✓
Perforation in the gallbladder <ul style="list-style-type: none"> <li>hole in the digestive organ that stores bile</li> </ul>		✓	✓

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 (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.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:

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

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

Keep out of reach and sight of children.

## If you want more information about AYBINTIO:

- 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 Canadian distributor (Organon Canada Inc.) website [www.organon.ca](http://www.organon.ca), or by calling 1-844-820-5468.

This leaflet was prepared by Samsung Bioepis Co., Ltd.

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