

Bevacizumab (Avastin®)

Pronounce: BEV-a-SIZ-oo-mab

Classification: Monoclonal Antibody

About Bevacizumab (Avastin®)

Monoclonal antibodies are created in a lab to attach to the targets found on specific types of cancer cells. The antibody "calls" the immune system to attack the cell it is attached to, resulting in the immune system killing the cell. These antibodies can work in different ways, including stimulating the immune system to kill the cell, blocking cell growth or other functions necessary for cell growth.

Bevacizumab is a monoclonal antibody that binds to and inhibits the activity of vascular endothelial growth factor (VEGF). This prevents the VEGF from interacting with its receptor on endothelial cells (lining of blood vessel). This, in turn, inhibits the formation of new blood vessels, which slows down the growth of the particular tissue. In essence, it kills tumors by cutting off their blood supply.

How to Take Bevacizumab (Avastin®)

Bevacizumab is given by intravenous (IV, into a vein) infusion. The amount of time the infusion will take will depend on your treatment plan and if you tolerate the medication. Dosage depends on the person's size and type of cancer being treated. How often you receive this medication and what other medications you receive will be determined by your care team.

Possible Side Effects of Bevacizumab (Avastin®)

There are a number of things you can do to manage the side effects of bevacizumab. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

High Blood Pressure

Patients receiving bevacizumab can develop high blood pressure (hypertension). Your blood pressure should be monitored at every clinic visit or every 2-3 weeks. If your blood pressure is elevated, you may be treated with a medication to reduce your pressure. If severe hypertension develops, bevacizumab should be discontinued immediately. Your blood pressure should continue to be monitored, even if bevacizumab is stopped. Signs of hypertension to report to your team include: blurry vision, nosebleed, headache and fatigue.

Fatigue

Fatigue is very common during cancer treatment and is an overwhelming feeling of exhaustion that is not usually relieved by rest. While on cancer treatment, and for a period after, you may need to adjust your schedule to manage fatigue. Plan times to rest during the day and conserve energy for more important activities. Exercise can help combat fatigue; a simple daily walk with a friend can help. Talk to your healthcare team for helpful tips on dealing with this side effect.

Bleeding

Patients may experience minor bleeding, such as a nosebleed. Serious bleeding has also occurred in patients treated with this medication, including coughing up blood, bleeding into the stomach, vomiting blood, bleeding

in the brain (stroke), and vaginal bleeding. People who have had serious bleeding should not take this medication. These events are uncommon, though if they occur, bevacizumab should be discontinued. While a nosebleed may not seem like much of a concern, you should notify your healthcare team right away if you develop bleeding of any sort.

Important but Less Common Side Effects

- **Wound Healing:** This medication can lead to slower or incomplete wound healing, such as a surgical wound not healing or staying closed. Therefore, it is recommended that the medication be discontinued 4 weeks prior to any surgery. In addition, the medication should be held for 28 days after surgery and any surgical incision should be fully healed prior to starting or restarting the medication. If you have a surgical wound that has not healed or begins to have signs of infection (redness, swelling, warmth), report this to your healthcare team.
- **Kidney Damage:** Kidney damage can occur while receiving bevacizumab. Your healthcare team will monitor this by periodically checking the amount of protein in your urine. If the protein levels become elevated, you may require further urine tests to evaluate your kidney function. If your kidneys become damaged, you may need to stop receiving this medication
- **Blood Clots, Stroke and Heart Attack:** Bevacizumab can increase the risk of blood clots, stroke and heart attack. If you experience symptoms of these problems, you should contact your healthcare provider immediately or go to an emergency room. Symptoms can include: swelling, redness or pain in an extremity, chest pain or pressure, pain in your arm, back, neck or jaw, shortness of breath, numbness or weakness on one side of the body, trouble talking, confusion or mental status changes.
- *Infusion Reactions:* The infusion can cause a reaction that may lead to chills, fever, low blood pressure, nausea and vomiting. Reactions are most common during the first week of therapy, including the evening after the infusion. Let your nurse know if you are feeling any different during your infusion.
- **Gastrointestinal Perforation:** This medication can cause a tear in the intestinal wall, also called a gastrointestinal perforation. Signs of this can include: new or worsening pain in the abdomen, new abdominal swelling, chills, fever, constipation, nausea or vomiting. If you experience any of these, contact your healthcare provider immediately or go to the emergency room.
- **Posterior Reversible Encephalopathy Syndrome (PRES):** In rare cases, this medication has caused a neurological disorder called posterior reversible encephalopathy syndrome (PRES), also called reversible posterior leukoencephalopathy (RPLS). Symptoms of PRES/RPLS include headache, seizure, lethargy, confusion, blindness and other visual and neurological disturbances. Report any of these symptoms to your healthcare team immediately.
- *Fistula:* A possible, but rare, side effect is the development of a fistula, which is an abnormal passage between two body parts (for instance, a hole between the lung and esophagus).
- Congestive Heart Failure (CHF): Bevacizumab can cause or worsen pre-existing heart problems, including congestive heart failure. Notify your healthcare provider if you have sudden weight gain or swelling in the ankles or legs. If you develop chest pain or pressure, sweating, shortness of breath, nausea, dizziness or lightheadedness, call 911 or go to the nearest emergency room.

Sexual & Reproductive Concerns

This drug may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and vaginal dryness. In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective birth control is necessary during treatment and for at least 6

months after treatment, even if your menstrual cycle stops or you believe you are not producing sperm. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your oncology team. You should not breastfeed while taking this medication and for 6 months after treatment.

Current Biosimilars

There are biosimilar versions of bevacizumab. A biosimilar is a medication that has been approved by the FDA because it is very similar to an FDA-approved medication (called a reference product, or the medication it is being compared to), and that there are no meaningful differences between the biosimilar product and the reference product. These medications may be used interchangeably.

The biosimilar versions of this medication include bevacizumab-awwb (Mvasi), bevacizumab-bvzr (Zirabev®) bevacizumab-tnjn (Avzivi), bevacizumab-adcd (Vegzelma), and bevacizumab-maly (Alymsys).

Cisplatin (Platinol®)

Pronounce: SIS-plat-in

Classification: Platinum Coordination Complex

About Cisplatin (Platinol®)

Cisplatin is a heavy metal compound that inhibits synthesis of RNA, DNA, and protein in cells. All of these compounds are vital for cells to divide and grow. By preventing them from dividing, the medication can stop cancer from growing.

How to Take Cisplatin

Cisplatin is given through intravenous (IV, into a vein) infusion. The dose and schedule are determined by your size and type of cancer. You will be given IV fluids prior to receiving cisplatin. It can be given alone or with other drugs.

Even when carefully and correctly administered by trained personnel, this drug may cause a feeling of burning and pain. There is a risk that this medication may leak out of the vein at the injection site, resulting in tissue damage that can be severe. If the area of injection becomes red, swollen, or painful at anytime <u>during or after</u> the injection, notify your care team right away. Do not apply anything to the site unless told to do so by your care team.

This medication can affect the blood levels of some anti-seizure medications. Be sure to tell your healthcare provider about all medications and supplements you take.

Possible Side Effects

There are a number of things you can do to manage the side effects of cisplatin. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Kidney Problems

This medication can cause kidney problems, including an increased creatinine level, which your oncology care team will monitor for using blood tests. Notify your healthcare provider if you notice decreased urine output, blood in the urine, swelling in the ankles, or loss of appetite.

Peripheral Neuropathy (Numbness or Tingling in the Hands and/or Feet)

Peripheral neuropathy is a toxicity that affects the nerves. It causes numbness or a tingling feeling in the hands

and/or feet, often in the pattern of a stocking or glove. This can get progressively worse with additional doses of the medication. In some people, the symptoms slowly resolve after the medication is stopped, but for some it never goes away completely. You should let your care team know if you experience numbness or tingling in the hands and/or feet, as they may need to adjust the doses of your medication.

Nausea and/or Vomiting

Talk to your oncology care team so they can prescribe medications to help you manage nausea and vomiting. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Low White Blood Cell Count (Leukopenia or Neutropenia)

White blood cells (WBC) are important for fighting infection. While receiving treatment, your WBC count can drop, putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- Washing hands, both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bathe daily and perform frequent mouth care.
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with has any vaccinations.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the red cell count is low, you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the count is low you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib) etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding use of these agents and all over the counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Hearing Problems

Cisplatin can cause hearing loss and ringing in the ears. Your hearing will be checked prior to you receiving cisplatin and as needed throughout treatment. Call your doctor or nurse if you have ringing in your ears or if you notice a decrease in your hearing.

Allergic Reactions

In some cases, patients can have an allergic reaction to this medication. Signs of a reaction can include: shortness of breath or difficulty breathing, chest pain, rash, flushing or itching or a decrease in blood pressure. If you notice any changes in how you feel during the infusion, let your nurse know immediately. The infusion will be slowed or stopped if this occurs. Depending on the severity of your reaction, you may still be able to receive the medication with a pre-medication to prevent a reaction, or if the medication is given at a slower rate.

Important but Less Common Side Effects

- **Electrolyte Abnormalities:** This medication can affect the normal levels of electrolytes (potassium, magnesium, calcium, etc.) in your body. Your levels will be monitored using blood tests. If your levels become too low, your care team may prescribe specific electrolytes to be given by IV or taken by mouth. Do not take any supplements without first consulting with your care team.
- Taste and Smell Changes: You may experience a metallic taste or find that food has no taste at all. You may dislike foods or beverages that you liked before receiving cancer treatment. These symptoms can last for several months or longer after treatment ends. Avoid any food that you think smells or tastes bad. If red meat is a problem, eat chicken, turkey, eggs, dairy products, and fish without a strong smell. Sometimes cold food has less of an odor. Add extra flavor to meat or fish by marinating it in sweet juices, sweet and sour sauce, or dressings. Use seasonings like basil, oregano or rosemary to add flavor. Bacon, ham, and onion can add flavor to vegetables. Ask your nurse about nutritional counseling services to help with food choices.
- **Vision Changes:** This medication can cause blurred vision and a change in color perception, especially with higher doses or increased frequency of doses. Report any vision changes to your healthcare team immediately.
- **Secondary Cancers:** A secondary cancer is one that develops as a result of cancer treatment for another cancer. This is quite rare, but you should be aware of the risk. In most cases, a secondary cancer related to chemotherapy is a blood cancer (leukemia, lymphoma). This can occur years after treatment. This is most often associated with repeated treatments or high doses. Your provider will monitor your labs closely. Consider having a complete blood count with differential checked annually by your healthcare provider if you received high risk therapies.
- Posterior Reversible Encephalopathy Syndrome (PRES): In rare cases, this medication has caused
 a neurological disorder called posterior reversible encephalopathy syndrome (PRES), also called
 reversible posterior leukoencephalopathy (RPLS). Symptoms of PRES/RPLS include headache, seizure,
 lethargy, confusion, blindness, and other visual and neurological disturbances. Report any of these
 symptoms to your healthcare team immediately.

Reproductive Concerns

This medication may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and vaginal dryness. In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. For women, effective birth control is necessary during treatment and for at least 14 months after treatment, even if your menstrual cycle stops. For men, effective birth control is

necessary during treatment and for at least 11 months after treatment, even if you believe you are not producing sperm. You should consult with your healthcare team before breastfeeding while receiving this medication.

Gemcitabine (Gemzar®)

Pronounce: jem-SYE-ta-been

Classification: Antimetabolite

About Gemcitabine (Gemzar®)

Gemcitabine is a type of medication called an "antimetabolite." Antimetabolites affect the DNA of cancer cells, leading to the slowing or stopping of cancer. Since cancer cells divide faster and with less error-correcting than healthy cells, cancer cells are more sensitive to this damage than normal cells.

How to Take Gemcitabine

Gemcitabine is given by intravenous (IV, into a vein) infusion. The dosage and scheduledepends on your size and type of cancer. It can be given alone or with other medications or therapies, such as radiation.

When given at the same time as radiation, there can be more side effects. At least one week should pass between the start or end of radiation therapy and a full gemcitabine dose. Please make sure all your healthcare providers are aware of your treatment history with gemcitabine and/or radiation.

Patients may have gemcitabine toxicity if the medication is infused for more than 60 minutes or if the medication is given more than once a week. Side effects of toxicity can include severe flu-like symptoms, fever, low blood pressure, and low blood counts. If you have any of these side effects, let your provider know. You may be told to take medication to manage these side effects and you will be closely monitored for toxicity.

Possible Side Effects of Gemcitabine

There are a number of things you can do to manage the side effects of gemcitabine. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Nausea and/or Vomiting

Talk to your oncology care team so they can prescribe medications to help you manage nausea and vomiting. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Liver Toxicity

This medication can cause liver toxicity, which your provider will monitor for using blood tests called liver function tests. Tell your healthcare provider if you notice yellowing of the skin or eyes, if your urine appears dark or brown, or if you have pain in your abdomen (belly), as these can be signs of liver toxicity.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the red cell count is low, you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing, or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low White Blood Cell Count (Leukopenia or Neutropenia)

White blood cells (WBC) are important for fighting infection. While receiving treatment, your WBC count can drop, putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F/38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- Washing hands, both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever, or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bathe daily and perform frequent mouth care.
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with has any vaccinations.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the count is low you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums, or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib), etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding the use of these agents and all overthe-counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Rash

Some patients may develop a rash, dry skin, or itching. This rash can become severe, so be sure to let your care team know if you develop a rash. Use an alcohol-free moisturizer on your skin and lips; avoid moisturizers with perfumes or scents. Your doctor or nurse can recommend a topical medication if itching is bothersome. If your skin does crack or bleed, be sure to keep the area clean to avoid infection. Be sure to notify your healthcare provider of any rash that develops, as this can be a reaction. They can give you more tips on caring for your skin.

Fluid Retention / Swelling

Some patients may develop fluid retention, which can cause swelling in the feet and/or ankles or face or gain weight. Fluid can also build up in the lungs and cause you to feel short of breath. Notify your healthcare team if you have any swelling, unexpected weight gain, or shortness of breath.

Important but Less Common Side Effects

• **Lung Problems:** This medication may cause pulmonary fibrosis (a scarring and stiffening of the lung tissue), interstitial pneumonitis, pulmonary edema, or acute respiratory distress syndrome (ARDS). These problems can develop during treatment or up to two weeks after treatment is completed. Call

your physician right away if you have shortness of breath, cough, wheezing, or difficulty breathing.

- **Posterior Reversible Encephalopathy Syndrome (PRES):** PRES is a rare, reversible neurological disorder that can occur with the use of gemcitabine. Symptoms of PRES include seizure, high blood pressure, headache, confusion, fatigue, confusion, any changes in your vision, or difficulty walking or thinking. If you experience any of these symptoms, contact your care team or go to the emergency room immediately.
- **Hemolytic Uremic Syndrome (HUS):** This medication can also cause a rare complication called hemolytic uremic syndrome (HUS). Your healthcare team will monitor you for symptoms of HUS throughout your treatment. Notify your healthcare team if you notice changes in the color or amount of your urine or if you develop bleeding or increased bruising.
- Capillary Leak Syndrome: Capillary leak syndrome is a condition in which blood and components of blood leak out of vessels and into body cavities and muscles. The movement of this fluid out of the vessels can cause hypotension (low blood pressure) and organ failure. Signs and symptoms of capillary leak syndrome include a sudden drop in blood pressure, weakness, fatigue, sudden swelling of the arms, legs, or other parts of the body, nausea, and lightheadedness. If you are having any of these symptoms notify your infusion nurse or provider immediately.
- **Radiation Recall:** Radiation recall is when the administration of a medication causes a skin reaction that looks like a sunburn (redness, swelling, soreness, peeling skin) in areas where radiation was previously given. Notify your oncology team if you notice this side effect. Treatment can include topical steroid ointments and a delay in your next chemotherapy dose.
- Severe cutaneous adverse reactions (SCARs), including Stevens Johnson Syndrome and toxic epidermal necrolysis (TEN): This medication can cause rare, but serious allergic reactions that affect the skin and mucous membranes. These skin reactions often start as a rash or painful blister and can progress (get worse) to serious damage to the skin and, in some cases, death. If you notice a new rash, have a fever and flu-like symptoms, lesions on mucuous membranes, or swollen lymph nodes, call your care team right away.

Reproductive Concerns

This medication may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and vaginal dryness. In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. For women, effective birth control is necessary during treatment and for 6 months after your last dose. For men, effective birth control is necessary during treatment and for 3 months after your last dose. Even if your menstrual cycle stops or you believe you are not producing sperm, you could still be fertile and conceive. You should not breastfeed while receiving this medication or for 1 week after your final dose.

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