# For the Patient: GUAVPEMAX6

**Other Names:** Treatment of Metastatic Renal Cell Carcinoma using 6-Weekly Pembrolizumab and Axitinib

**GU** = **G**enito**U**rinary
**AV** = **A**d**V**anced
**PEM** = **PEM**brolizumab
**AX** = **AX**itinib
**6** = every **6** weeks

## ABOUT THIS MEDICATION COMBINATION

### What is this treatment used for?

- GUAVPEMAX is a kidney cancer treatment using an intravenous (through the vein) drug called pembrolizumab (pem broe LIZ ue mab) and an oral (taken by mouth) drug called axitinib (ax i' ti nib).

### How does this treatment work?

- Pembrolizumab is a type of therapy called immunotherapy. It is an antibody designed to help your own body's immune system target cancer cells to stop them from growing.
- Axitinib works by interfering with certain enzymes called tyrosine kinases that are important in transmitting the chemical signals needed for essential processes like cell division and replication in cancer cells.

## INTENDED BENEFITS

- This treatment is being given to slow down the growth and destroy of your cancer cells in your body. This treatment can help to control some of the symptoms that cancer may be causing and may delay or prevent new symptoms from starting.

## TREATMENT SUMMARY

### How is this regimen given?

- Pembrolizumab will be given to you as an infusion (a drip) into a vein (intravenously)
- You will be treated with pembrolizumab once every 6 weeks. This 6 weeks period is called a "cycle". The cycle is repeated as long as you are benefiting from treatment and not having too many side effects up to a maximum of 18 cycles or 2 years.
- Axitinib is taken by mouth twice a day, continuously, as long as you are benefiting from treatment and not having too many side effects.
- Axitinib should be swallowed whole with a glass of water, and may be taken with food or on an empty stomach.

**What will happen while I am being treated?**

- A blood test is done within one month of starting treatment.
- A blood test is done before receiving each treatment cycle, usually at the time you see your oncologist.
- The dose of your treatment may be changed or held based on your blood test results and/or other side effects.

## OTHER INSTRUCTIONS

***It is very important to report side effects immediately to your doctor. Do not manage side effects at home without speaking with your doctor. Be aware that symptoms may be delayed and can develop months after your last dose. If other doctors are involved in your care it is important they know you are on these treatments and the autoimmune side effects they can cause.***

**What other drugs or foods can interact with GUAVPEMAX?**

- Other drugs may interact with pembrolizumab and/or axitinib. Check with your doctor or pharmacist before you start or stop taking any other drugs including all prescription and non-prescription medicines, steroids, vitamins, and herbal supplements.
- The drinking of alcohol (in small amounts) does not appear to affect the safety or usefulness of this treatment.

**Important things to know about pembrolizumab:**

- **Before you are given pembrolizumab**, talk to your doctor or pharmacist if you:
  - have an active condition where your immune system attacks your body (autoimmune disease), such as ulcerative colitis, Crohn's disease, lupus, rheumatoid arthritis or sarcoidosis.
  - take other medicines that make your immune system weak. Examples of these may include steroids, such as prednisone or dexamethasone.
  - had an organ transplant, such as a kidney transplant.
  - have any other medical conditions.
- It is very important to tell your doctor immediately if you have, or develop, any of the symptoms listed under **Serious Side Effects. Do not try to treat or diagnose symptoms yourself.**
- You may have a **transient worsening of disease** before the tumour shrinks.
- Pembrolizumab may damage sperm and may harm the baby if used during pregnancy. You must use **birth control** while being treated with pembrolizumab and for at least **4 months** after your last dose. Tell your doctor right away if you or your partner becomes pregnant.
- Pembrolizumab may pass into your breast milk. **Do not breastfeed** during treatment
- ***Tell*** doctors or dentists that you are being treated with pembrolizumab before you receive any treatment from them. You should carry the BC Cancer ***wallet card*** for pembrolizumab to alert health providers.
- ***Do not receive any immunizations before discussing with your doctor***

**Important things to know about axitinib:**

- It is very important to tell your doctor or get emergency help immediately if you have:
  - Signs of **stroke** such as sudden onset of severe headache, eyesight changes, slurred speech, loss of coordination, weakness or numbness in arm or leg.
  - Signs of **infection** such as fever (over 100°F or 38°C by an oral thermometer), shaking chills; severe sore throat, productive couth (coughing up thick or green sputum); cloudy or foul-smelling urine; painful, tender, or swollen red skin wounds or sores.
  - Signs of **bleeding problems** such as black, tarry stools; blood in urine; pinpoint red spots on skin; extensive bruising; coughing up blood, or nosebleeds.
  - Signs of **blood clot** such as tenderness or hardness over a vein, calf swelling and tenderness, sudden onset of cough, chest pain, or shortness of breath.
- Axitinib may damage sperm and may harm the baby if used during pregnancy. You must use **birth control** while being treated with axitinib. Tell your doctor right away if you or your partner becomes pregnant.
- Axitinib may pass into your breast milk. **Do not breastfeed** during treatment.
- ***Tell*** doctors or dentists that you are being treated with pembrolizumab before you receive any treatment from them. If you are planning to have **surgery**, you should stop taking axitinib 24 hours prior to surgery. Do not restart axitinib until the surgical wound is fully healed. This helps to lower the risk of bleeding and may prevent problems with wound healing after surgery.

## SIDE EFFECTS AND WHAT TO DO ABOUT THEM

**Are there any risks?**
Unexpected and unlikely side effects can occur with any drug treatment. The ones listed below are particularly important for you to be aware of as they are directly related to the common actions of the drug in your treatment plan.

**What is the most important information I should know about SERIOUS SIDE EFFECTS?**

- **Pembrolizumab may cause serious immune reactions against your own body (autoimmune) affecting many parts.**
- The following side effects were most frequently reported:
  - diarrhea
  - itching, rash
  - joint pain
  - feeling tired
  - feeling less hungry
  - cough
- These side effects are most likely to begin during treatment; however, side effects can show up months after your last treatment with pembrolizumab.
- ***Tell*** your doctor as soon as possible if you have any of serious side effects listed in the table below or your symptoms get worse.
- **Do not try to treat or diagnose symptoms yourself**. Getting medical treatment right away may keep the problem from becoming more serious.

## SERIOUS SIDE EFFECTS (IMMUNE RELATED) ASSOCIATED WITH PEMBROLIZUMAB

| SERIOUS SIDE EFFECTS | How common is it? |
|---|---|
| **Inflammation of the intestines (colitis)**<br>*Symptoms may include:*<br>• diarrhea (loose stools) or more bowel movements than usual. **Do not treat the diarrhea yourself.**<br>• blood or mucus in stools or dark, tarry, sticky stools<br>• severe stomach pain (abdominal pain) or tenderness | Common<br><br>(less than 1 in 10 but more than 1 in 100) |
| **Inflammation of the thyroid gland (hyperthyroidism, hypothyroidism)**<br>*Symptoms may include:*<br>• rapid heart beat<br>• weight loss or gain<br>• increased sweating<br>• hair loss<br>• feeling cold<br>• constipation or diarrhea<br>• your voice gets deeper<br>• muscle aches<br>• changes in sleep patterns | Common<br><br>(less than 1 in 10 but more than 1 in 100) |
| **Inflammation of the pituitary gland (hypophysitis, hypopituitarism, including secondary adrenal insufficiency)**<br>*Symptoms may include:*<br>• weight loss<br>• increased sweating, hot flashes<br>• hair loss (includes facial and pubic)<br>• feeling cold<br>• headaches that will not go away or unusual headache<br>• decreased sex drive<br>• vision problems<br>• excessive thirst and urination | Common<br><br>(less than 1 in 10 but more than 1 in 100) |

| SERIOUS SIDE EFFECTS | How common is it? |
|---|---|
| **Inflammation of the lungs (pneumonitis)**<br>*Symptoms may include:*<br>• shortness of breath<br>• chest pain<br>• coughing | Common<br><br>(less than 1 in 10 but more than 1 in 100) |
| **Problems with muscles**<br>*Symptoms may include:*<br>• back pain<br>• spasms<br>• weakness<br>• muscle pain | Common<br><br>(less than 1 in 10 but more than 1 in 100) |
| **Skin problems**<br>*Symptoms may include:*<br>• rash<br>• dry skin | Common<br><br>(less than 1 in 10 but more than 1 in 100) |
| **Problems in other organs (nervous system, eyes)**<br>*Symptoms may include:*<br>• tingling, numbness, lack of energy<br>• changes in eyesight<br>• dizziness | Common<br><br>(less than 1 in 10 but more than 1 in 100) |
| **Inflammation of the liver (hepatitis)**<br>*Symptoms may include:*<br>• nausea or vomiting<br>• loss of appetite<br>• pain on the right side of your stomach<br>• yellowing of your skin or the whites of your eyes<br>• dark urine<br>• bleeding or bruise more easily than normal | Uncommon<br><br>(less than 1 in 100 but more than 1 in 1000) |

| SERIOUS SIDE EFFECTS | How common is it? |
|---|---|
| **Inflammation of the kidneys (nephritis)**<br>*Symptoms may include:*<br>• changes in the amount or colour of your urine | Uncommon<br><br>(less than 1 in 100 but more than 1 in 1000) |
| **Problems in the pancreas**<br>*Symptoms may include:*<br>• abdominal pain<br>• nausea and vomiting | Rare<br><br>(less than 1 in 1000 but more than 1 in 10000) |
| **Blood sugar problems (type 1 diabetes mellitus)**<br>*Symptoms may include:*<br>• hunger or thirst<br>• a need to urinate more often<br>• weight loss | Rare<br><br>(less than 1 in 1000 but more than 1 in 10000) |
| **Infusion reactions**<br>*Symptoms may include:*<br>• shortness of breath<br>• itching or rash<br>• dizziness<br>• fever<br>• wheezing<br>• flushing<br>• feeling like passing out | Rare<br><br>(less than 1 in 1000 but more than 1 in 10000) |

## MANAGEMENT OF NON-IMMUNE RELATED SIDE EFFECTS ASSOCIATED WITH PEMBROLIZUMAB AND AXITINIB

| OTHER SIDE EFFECTS | How common is it? | MANAGEMENT |
|---|---|---|
| Your **white blood cells** may decrease during your treatment. White blood cells protect your body by fighting bacteria (germs) that cause infection. **When they are low, you are at greater risk of having an infection.** | Sometimes | To help prevent infection:<br>• Wash your hands often and always after using the bathroom.<br>• Avoid crowds and people who are sick.<br>• Call your doctor ***immediately*** at the first sign of an infection such as fever (over 100°F or 38°C by an oral thermometer), chills, cough, or burning when you pass urine. |
| Your **platelets** may decrease during your treatment. Platelets help to make your blood clot when you hurt yourself. **You may bruise or bleed more easily than usual.** | Sometimes | To help prevent bleeding problems:<br>• Try not to bruise, cut, or burn yourself.<br>• Clean your nose by blowing gently. Do not pick your nose.<br>• Avoid constipation.<br>• Brush your teeth gently with a soft toothbrush as your gums may bleed more easily. Maintain good oral hygiene.<br>• Some medications such as ASA (e.g., ASPIRIN®) or ibuprofen (ADVIL®) may increase your risk of bleeding.<br>• Do not stop taking any medications that has been prescribed by your doctor (e.g. ASA for your heart).<br>• For minor pain, try acetaminophen (e.g. TYLENOL®), to a maximum of 4 g (4000 mg) per day. |
| **High blood pressure** may sometimes occur. This can happen very quickly after starting treatment. | Sometimes | • Your blood pressure will be checked during your visits to your doctor.<br>• You may be asked to check your blood pressure frequently between visits.<br>• Your doctor may give you medication if your blood pressure is high.<br>• Tell your doctor if you are already on blood pressure medication. Your doctor may have to adjust your dose. |

| OTHER SIDE EFFECTS | How common is it? | MANAGEMENT |
|---|---|---|
| **Sore mouth** may sometimes occur a few days after treatment. Mouth sores can occur on the tongue, the sides of the mouth, or in the throat. **Mouth sores or bleeding gums can lead to an infection.** | Sometimes | • Brush your teeth gently after eating and at bedtime with a very soft toothbrush. If your gums bleed, use gauze instead of a brush. Use baking soda instead of toothpaste.<br>• Make a mouthwash with ½ teaspoon baking soda or salt in 1 cup of warm water and rinse several times a day.<br>• Try the ideas in *Food Ideas to Try with a Sore Mouth.** |
| **Hand-foot skin reaction** may sometimes occur during treatment. The palms of your hands and soles of your feet may tingle become red numb, painful, or swollen. Skin may also become dry or itchy. You may not be able to do your normal daily activities if blisters, severe pain, or ulcers occur. | Sometimes | • Avoid tight-fitting shoes or rubbing pressure to hands and feet, such as that caused by heavy activity.<br>• Avoid tight-fitting jewellery.<br>• Clean hands and feet with lukewarm water and gently pat to dry; avoid hot water.<br>• Apply a sunscreen with SPF (sun protection factor) of at least 30.<br>• Apply lanolin-containing creams (e.g., BAG BALM®, UDDERLY SMOOTH®) to hands and feet, liberally and often.<br>• Tell your cancer doctor or your nurse at the next visit if you have any signs of hand-foot skin reaction as your dose may need to be changed. |
| **Nausea** and **vomiting** may occur after your treatment. Most people have little or no nausea. | Rare | • You may be given a prescription for antinausea drug(s) to take before your treatment and/or at home. **It is easier to prevent nausea than treat it once it has occurred**, so follow directions closely.<br>  ○ Drink plenty of fluids.<br>  ○ Eat and drink often in small amounts.<br>• Try the ideas in *Food Choices to Help Control Nausea.**<br>• If nausea and vomiting is persistent and you have other symptoms of **hepatitis**, tell your doctor as soon as possible. (see the table above for serious side effects.) |

| OTHER SIDE EFFECTS | How common is it? | MANAGEMENT |
|---|---|---|
| **Constipation** may sometimes occur. | Sometimes | • Exercise if you can.<br>• Drink plenty of fluids.<br>• Try ideas in *Suggestions for Dealing with Constipation*.*<br>• If you have other symptoms of **colitis**, tell your doctor as soon as possible. (see the table above for serious side effects.) |
| **Fever** may sometimes occur. | Sometimes | • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day.<br>• If you have other symptoms of **colitis**, tell your doctor as soon as possible. (see the table above for serious side effects.) |
| **Headache** may sometimes occur. | Sometimes | • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours if needed, to a maximum of 4 g (4000 mg) per day.<br>• If headache is persistent and you have other symptoms of **inflammation of glands or Inflammation of the nerves**, tell your doctor as soon as possible. (see the table above for serious side effects.) |
| **Loss of appetite** and **weight loss** sometimes occur. | Sometimes | • Try the ideas in *Food Ideas to Help with Decreased Appetite.*<br>• If loss of appetite is persistent and you have other symptoms of **hepatitis**, tell your doctor as soon as possible. (see the table above for serious side effects.) |
| **Hair loss** is rare with pembrolizumab and axitinib. | Rare | • If hair loss is a problem, refer to *For the Patient: Hair Loss Due to Chemotherapy*.* |
| **Pain** or **tenderness** may occur where the needle was placed. | Very rare | Apply cool compresses or soak in cool water for 15-20 minutes several times a day. |

***Please ask your oncologist or pharmacist for a copy.**

**If you experience symptoms or changes in your body that have not been described above but worry you, or in any symptoms are severe, contact:**

**_____ at telephone number:_____**

BC CANCER
Provincial Health Services Authority

MEDICAL ALERT

NAME _____

has received

CHECKPOINT INHIBITOR IMMUNOTHERAPY:

Immune-Mediated Adverse Reactions

ALWAYS CARRY THIS CARD AND SHOW TO PHYSICIANS INCLUDING ANESTHETISTS

SEVERE IMMUNE-MEDIATED ADVERSE REACTIONS

Including enterocolitis, intestinal perforation, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, endocrinopathy, pneumonitis, myositis, myocarditis and toxicities in other organ systems. Duration of risk after treatment is unknown.

FOR MORE INFORMATION:

BC Cancer – Abbotsford .....604-851-4710
BC Cancer - Kelowna..... .....250-712-3900
BC Cancer - Prince George.....250-645-7300
BC Cancer - Surrey ..... .....604-930-4055
BC Cancer - Vancouver.....604-877-6000
BC Cancer - Victoria.....250-519-5500
www.bccancer.bc.ca/health-professionals/professional-resources/cancer-drug-manual

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To Whom It May Concern:

RE: _____

Medical Oncologist _____

Immunotherapy Regimen _____

This patient is receiving **immunotherapy** at the BC Cancer and is at risk of **immune-related toxicities** which may be life threatening and require urgent management.

Immunotherapy toxicities are different from those encountered with standard chemotherapy or targeted therapies. The immune system may become dysregulated during immunotherapy treatment, leading to symptoms and findings which mimic autoimmune disorders. Adverse events can occur during or following treatment and can be life threatening. Any organ system in the body is at risk including, but not limited to:

Lungs (pneumonitis, pleuritis, sarcoidosis)
Gastrointestinal (colitis, ileitis, pancreatitis)
Liver (hepatitis)
Skin (rash, Stevens-Johnson syndrome)
Endocrine (hypophysitis, adrenal insufficiency, hypo/hyperthyroidism, type 1 diabetes mellitus)
Renal (interstitial nephritis)
Blood (hemolytic anemia, thrombocytopenia, neutropenia)
Neurologic (encephalitis, Guillain-Barré syndrome, meningitis, myasthenia gravis, neuropathy)
Musculoskeletal (myositis, arthritis)
Cardiovascular (pericarditis, myocarditis, vasculitis)
Ophthalmologic (uveitis, scleritis, episcleritis, conjunctivitis, retinitis)

Management of immune-related toxicities necessitates prompt coordination with a medical oncologist with **initiation of high dose corticosteroids**, and may require referral to the appropriate subspecialty. If you suspect your patient is presenting with immune-related toxicity, **please contact the patient's medical oncologist** directly or if after hours contact the on-call physician, or as per your local centre's process (next page). Additional information on immunotherapy toxicity treatment algorithms is located at the end of the above posted protocol at www.bccancer.bc.ca.