

For the Patient: **GIAVPEM**

Other Names: First-Line Treatment of dMMR/MSI-H Metastatic Colorectal Cancer with Pembrolizumab

GI = GastroIntestinal
AV = AdVanced
PEM = PEMbrolizumab

ABOUT THIS MEDICATION

What is this drug used for?

- Pembrolizumab is an intravenous (through the vein) drug given to treat cancer of colon or rectum.

How does this drug work?

- Pembrolizumab is a type of therapy called immunotherapy. It is a monoclonal antibody, a type of protein designed to help your own body's immune system target cancer cells to stop them from growing.

INTENDED BENEFITS

- This treatment is being given to slow down the growth 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 drug given?

- Pembrolizumab is a clear liquid given as an infusion directly into the vein (IV).
- You will receive pembrolizumab at the clinic by a chemotherapy nurse, for one day only. Your treatment will last about 30-60 minutes. Your first treatment will probably take longer, as the nurse will review information on the chemotherapy drug with you. *It is a good idea to bring someone with you to your first treatment appointment.*
- The treatment is repeated every 3 weeks. This 3 week period of time is called a "cycle". This treatment will continue for a maximum of 35 cycles as long as you are benefiting from treatment and not having too many side effects, as determined by your oncologist.

The calendar on the following page shows how the medication is given each 3 week cycle.

C Y C L E 1	DATE	TREATMENT PLAN
		▶ Week 1 → Pembrolizumab IV on day 1 only
		▶ Weeks 2 + 3 → no treatment

C Y C L E 2	DATE	TREATMENT PLAN
		▶ Week 1 → Pembrolizumab IV on day 1 only
		▶ Weeks 2+3 → no treatment

Treatment is continued for a maximum of 35 cycles as long as you are benefiting from treatment and not having too many side effects.

What will happen while I am being treated?

- A blood test is done before starting each treatment cycle, usually at the time you see your oncologist.
- Your treatment may be interrupted based on your blood test results and/or other side effects.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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.

You doctor will review the risks of treatment and possible side effects with you before starting treatment. The chemotherapy nurse will review possible side effects of the drug and how to manage those side effects with you on the day you receive your first treatment.

Pembrolizumab may cause serious immune reactions against your own body (autoimmune) affecting many parts.

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

- Pembrolizumab can cause serious side effects in many parts of your body. 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 DURING TREATMENT	How Common is it?
<p>Inflammation of the intestines (colitis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • diarrhea (loose stools) or more bowel movements than usual. Do not treat the diarrhea yourself. • blood or mucus in stools or dark, tarry, sticky stools • severe stomach pain (abdominal pain) or tenderness 	<p>Common (less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the thyroid gland (hyperthyroidism, hypothyroidism) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • rapid heart beat • weight loss or gain • increased sweating • hair loss • feeling cold • constipation or diarrhea • your voice gets deeper • muscle aches • changes in sleep patterns 	<p>Common (less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the pituitary gland (hypophysitis, hypopituitarism, including secondary adrenal insufficiency) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • weight loss • increased sweating, hot flashes • hair loss (includes facial and pubic) • feeling cold • headaches that will not go away or unusual headache • decreased sex drive • vision problems • excessive thirst and urination 	<p>Common (less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the lungs (pneumonitis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • shortness of breath • chest pain • coughing 	<p>Common (less than 1 in 10 but more than 1 in 100)</p>

SERIOUS SIDE EFFECTS DURING TREATMENT	How Common is it?
Problems with muscles <i>Symptoms may include:</i> <ul style="list-style-type: none"> • rash • dry skin 	Common (less than 1 in 10 but more than 1 in 100)
Problems in other organs (nervous system, eyes) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • tingling, numbness, lack of energy • changes in eyesight • dizziness 	Common (less than 1 in 10 but more than 1 in 100)
Inflammation of the liver (hepatitis) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • nausea or vomiting • loss of appetite • pain on the right side of your stomach • yellowing of your skin or the whites of your eyes • dark urine • bleeding or bruise more easily than normal 	Uncommon (less than 1 in 100 but more than 1 in 1000)
Inflammation of the kidneys (nephritis) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • changes in the amount or colour of your urine 	Uncommon (less than 1 in 100 but more than 1 in 1000)
Problems in the pancreas <i>Symptoms may include:</i> <ul style="list-style-type: none"> • abdominal pain • nausea and vomiting 	Rare (less than 1 in 1000 but more than 1 in 10000)
Blood sugar problems (type 1 diabetes mellitus) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • hunger or thirst • a need to urinate more often • weight loss 	Rare (less than 1 in 1000 but more than 1 in 10000)
Infusion reactions <i>Symptoms may include:</i> <ul style="list-style-type: none"> • Shortness of breath, itching or rash, dizziness, fever, wheezing, flushing, feeling like passing out, chills and may sometimes occur during the first pembrolizumab infusion. • Reactions are less common with later treatments. • Tell your nurse or doctor immediately if you have a reaction during your treatment. • Your pembrolizumab may be temporarily stopped and then given more slowly. • You may be given other drugs to treat the reaction. 	Rare (less than 1 in 1000 but more than 1 in 10000)

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Pain or tenderness may occur where the needle was placed.</p>	<p>Apply cool compresses or soak in cool water for 15 – 20 minutes several times a day.</p>
<p>Nausea and vomiting may occur after your treatment.</p>	<p>You may be given a prescription for anti-nausea drug(s) to take before your chemotherapy treatment and/or at home. It is easier to prevent nausea than treat it once it has occurred, so follow directions closely.</p> <ul style="list-style-type: none"> • Drink plenty of fluids. • Eat and drink often in small amounts. • Try the ideas in <i>Practical Tips to Help Manage Nausea*</i> • 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.)
<p>Fever may sometimes occur.</p>	<ul style="list-style-type: none"> • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day. • If you have other symptoms of colitis, tell your doctor as soon as possible. (see the table above for serious side effects.)
<p>Constipation may sometimes occur.</p>	<ul style="list-style-type: none"> • Exercise if you can. • Drink plenty of fluids. • Try ideas in <i>Suggestions for Dealing with Constipation.*</i> • If you have other symptoms of colitis, tell your doctor as soon as possible. (see the table above for serious side effects.)
<p>Diarrhea may sometimes occur.</p>	<p>If diarrhea is a problem:</p> <ul style="list-style-type: none"> • Drink plenty of liquids. • Eat and drink often in small amounts • Avoid high fibre foods as outlined in <i>Food Ideas to Help Manage Diarrhea*</i> • If you have other symptoms of colitis, tell your doctor as soon as possible. (see the table above for serious side effects.)
<p>Headache may sometimes occur.</p>	<ul style="list-style-type: none"> • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day. • 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.)

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Loss of appetite and weight loss are common.	<ul style="list-style-type: none"> • Try the ideas in <i>Food Ideas to Help with Decreased Appetite</i>.* • 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.)
Tiredness and lack of energy may occur.	<ul style="list-style-type: none"> • Do not drive a car or operate machinery if you are feeling tired. • <i>Try the ideas in the handout titled Fatigue/Tiredness</i>* • If tiredness is persistent and you have other symptoms of hepatitis or inflammation of glands, tell your doctor as soon as possible. (see the table above for serious side effects.)
Hair loss is rare with pembrolizumab.	<ul style="list-style-type: none"> • If hair loss is a problem, refer to <i>Resources for Hair Loss and Appearance Changes</i>.*
You may sometimes have trouble sleeping.	<ul style="list-style-type: none"> • Talk to your doctor if you continue to have trouble sleeping. • This will return to normal when you stop taking pembrolizumab.

* Please ask your chemotherapy nurse, pharmacist or dietitian for a copy

INSTRUCTIONS FOR THE PATIENT

What other drugs or foods can interact with pembrolizumab?

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

Other important things to know:

- **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.
- This treatment may cause sterility in men and menopause in women. If you plan to have children, discuss this with your oncologist before starting treatment.
- This treatment may damage sperm and may cause harm to the baby if used during pregnancy. It is best to use birth control while you are undergoing treatment and for **4**

months after the last dose. Tell your doctor right away if you or your partner becomes pregnant. Do not breast feed during treatment.

- Tell all doctors including dentists you see that you are being treated with pembrolizumab before you receive treatment of any form.

THE FOLLOWING INFORMATION IS VERY IMPORTANT

SEE YOUR DOCTOR OR GET EMERGENCY HELP IMMEDIATELY IF YOU HAVE:

- Signs of an allergic reaction (rare) soon after a treatment including dizziness, fast heart beat, face swelling, or breathing problems.
- Signs of an infection such as fever (over 100°F or 38°C by an oral thermometer), shaking chills; severe sore throat, productive cough (coughing up thick or green sputum); cloudy or foul smelling urine; painful, tender, or swollen red skin wounds or sores.
- Diarrhea or changes in bowel habits; black, tarry stools; blood or mucous in the stool; severe abdominal pain.
- Signs of lung problems such as new or worsening cough, chest pain, coughing blood, shortness of breath, or difficulty in breathing.
- Signs of kidney problems such as lower back or side pain, blood in the urine, swelling of feet or lower legs, or change in amount or colour of urine.
- Signs of blood sugar problems such as thirst and frequent need to pass urine.

SEE YOUR DOCTOR AS SOON AS POSSIBLE (DURING OFFICE HOURS) IF YOU HAVE:

- Signs of anemia such as unusual tiredness or weakness.
- Signs of liver problems such as yellow eyes or skin, white or clay-coloured stools.
- Signs of thyroid problems such as unusual weight gain or loss, feeling hot or cold, deepened voice, or unusual tiredness or weakness.
- Changes in eyesight, eye pain, or redness.
- Skin rash, blisters, or itching.

CHECK WITH YOUR DOCTOR IF ANY OF THE FOLLOWING CONTINUE OR BOTHER YOU:

- Headache not controlled with acetaminophen (e.g., **TYLENOL®**).
- Changes in skin colour (lightening).
- Irritability or forgetfulness.
- Decreased sex drive.

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

_____ at telephone number: _____



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 - Abbotsford604-851-4710
- BC Cancer - Kelowna250-712-3900
- BC Cancer - Prince George.....250-645-7300
- BC Cancer - Surrey604-930-4055
- 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.

BC CANCER CENTRES	CONTACT INFORMATION AND PROCESS
Abbotsford	Contact the patient’s medical oncologist immediately by calling the Abbotsford Regional Hospital and Cancer Centre (ARHCC) switchboard at (604) 851-4700 and ask for the on-call medical oncologist (24-hour call system).
Kelowna	Between 8:30 am – 5:00 pm, call (250) 712-3900 (press “8” to speak to the Kelowna Centre receptionist) and have an oncologist paged. Outside these hours, call the Kelowna General Hospital switchboard at (250) 862-4000 and ask for the on-call medical oncologist.
Prince George	Between 8:30 am – 4:00 pm Monday to Friday, call (250) 645-7313. Outside these hours, go to the emergency department at the University Hospital of Northern British Columbia (UHNBC).
Surrey	Between 8:30 am – 4:00 pm Monday to Friday (except Statutory holidays), call the Nursing Phone Line at (604) 930-4053. Outside these hours, call the Surrey Memorial Hospital switchboard at (604) 581-2211 and ask for the Fraser Valley on-call medical oncologist.
Vancouver	Between 8:30 am – 4:30 pm Monday to Friday, call the Patient Nurse Line at (604) 877-6025. Outside these hours, call the inpatient unit at (604) 877-6000 and press 1, and ask for the on-call medical oncologist.
Victoria	Between 8:30 am – 4:30 pm Monday-Friday (except Statutory holidays), call (250) 519-5500, and press 1 then 4 to speak with a registered nurse. Outside these hours, call the Royal Jubilee Hospital switchboard at (250) 370-8000 and ask for the on-call medical oncologist.