

For the Patient: GOCXBP6

Other Names: BC Cancer Protocol for Maintenance Therapy of Squamous, Adenocarcinoma, or Adenosquamous Cancer of the Cervix with 6-Weekly Pembrolizumab with or without Bevacizumab

GO = Gynecologic Oncology
CX = Cervix
B = Bevacizumab
P = Pembrolizumab
6 = Given every 6 weeks

ABOUT THIS MEDICATION

What are these drugs used for?

- Pembrolizumab, with or without bevacizumab, is a drug given to treat some types of cancer including cervical cancer.

How do these drugs work?

- Pembrolizumab (pem" broe liz' ue mab) 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. Pembrolizumab is referred to as immunotherapy.
- Bevacizumab (be-va-SIZ-yoo-mab) is also a monoclonal antibody, designed to target and interfere with the growth of cancer cells.

INTENDED BENEFITS

- This treatment is being given to keep cancer from progressing, once it has been successfully controlled with initial chemotherapy treatment.

TREATMENT SUMMARY

How are these drugs given?

- Each medication will be given directly into the vein, intravenously (IV).
- The treatment will be given in 'cycles'. Each cycle length is 6 weeks.
- Pembrolizumab will be given on Day 1 every 6 weeks.
- If bevacizumab is part of your treatment, bevacizumab will be given two times in each 6-week cycle, on Day 1 and on Day 22.

- Pembrolizumab and bevacizumab will each take approximately 30 minutes to administer.
- Pembrolizumab will continue until 2 years of treatment, or when it is no longer helping, as determined by your oncologist.
- If bevacizumab is part of your treatment, it will continue until it is no longer helping, as determined by your oncologist.

The calendar below outlines your treatment plan.

If bevacizumab is part of your treatment:

Cycle 1:

		DATE	TREATMENT PLAN
C Y C L E 1			▶ Week 1 → Pembrolizumab and bevacizumab on Day 1
			Week 2 → no treatment
			Week 3 → no treatment
			Week 4 → Bevacizumab on Day 22
			Week 5 → no treatment
			Week 6 → no treatment

If bevacizumab is not part of your treatment:

Cycle 1:

		DATE	TREATMENT PLAN
C Y C L E 1			▶ Week 1 → Pembrolizumab and bevacizumab on Day 1
			Week 2 → no treatment
			Week 3 → no treatment
			Week 4 → no treatment
			Week 5 → no treatment
			Week 6 → no treatment

This treatment will continue every 6 weeks, until treatment is completed, as determined by your oncologist.

What will happen when I get my drugs?

- You will see your clinician and will need to have a blood test before each treatment.
- The dose and timing of your treatment may be changed based on your blood counts and/or other side effects.
- You may be given a prescription for anti-nausea medications (to be filled at your regular pharmacy). If you are given a prescription for them, please bring your anti-nausea medications with you for each treatment. Your nurse will tell you when to take the anti-nausea medication.
- You may also need to take anti-nausea drugs at home after therapy. It is easier to prevent nausea than to treat it once it has occurred, so follow directions closely.
- Your blood pressure will be checked by a nurse and a urine test will be done before each treatment. For the first three cycles, your blood pressure will be checked both before and after the bevacizumab infusion. The dose and timing of your therapy may be changed based on your blood pressure or urine test results.

OTHER INSTRUCTIONS:

It is very important to report side effects immediately to your doctor. Do not manage side effects at home without first 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.

INSTRUCTIONS:

- Tell your doctor if you have ever had an unusual or **allergic reaction** to pembrolizumab or bevacizumab before starting this treatment.
- The **drinking of alcohol** (in small amounts) does not appear to affect the safety or usefulness of treatment.
- Pembrolizumab and bevacizumab may harm the baby if used during pregnancy. It is best to use **birth control** while being treated with these drugs, and for at least 6 months after your last bevacizumab treatment, and 4 months after the last dose of pembrolizumab. Tell your doctor right away if you become pregnant. **Do not breastfeed** during treatment and for at least 4 months after the last dose of pembrolizumab.
- If you are planning to have **surgery**, you should stop bevacizumab 4 weeks before surgery and not restart bevacizumab until 4 weeks after surgery and only if the surgical wound is fully healed. This helps to lower the risk of bleeding and may prevent problems with wound healing after surgery.

- Tell doctors, dentists and other health professionals that you are being treated with pembrolizumab and bevacizumab 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**

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 significant medical conditions.

Medication Interactions:

- Other drugs may **interact** with pembrolizumab and bevacizumab. Tell a member of your healthcare team if you are taking any other drugs before starting treatment. Check with your doctor or pharmacist before you start or stop taking any drugs including all prescription and non-prescription medicines, steroids or other medicines that lower your immune response, vitamins, and herbal supplements.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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

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 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.

The following side effects were most frequently reported:

Very common (more than 1 in 10 people)

- diarrhea
- itching, rash
- joint pain
- feeling tired
- feeling less hungry
- cough

SERIOUS SIDE EFFECTS	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</p> <p>(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</p> <p>(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</p> <p>(less than 1 in 10 but more than 1 in 100)</p>

SERIOUS SIDE EFFECTS	How common is it?
<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</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Problems with muscles <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • back pain • spasms • weakness • muscle pain 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Skin problems <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • rash • dry skin 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Problems in other organs (nervous system, eyes) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • tingling, numbness, lack of energy • changes in eyesight • dizziness 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Blood sugar problems (type 1 diabetes mellitus) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • hunger or thirst • a need to urinate more often • weight loss 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the liver (hepatitis) <i>Symptoms may include:</i></p> <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 	<p>Uncommon</p> <p>(less than 1 in 100 but more than 1 in 1000)</p>
<p>Inflammation of the kidneys (nephritis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • changes in the amount or colour of your urine 	<p>Uncommon</p> <p>(less than 1 in 100 but more than 1 in 1000)</p>

SERIOUS SIDE EFFECTS	How common is it?
<p>Problems in the pancreas <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • abdominal pain • nausea and vomiting 	<p>Rare</p> <p>(less than 1 in 1000 but more than 1 in 10000)</p>
<p>Infusion reactions <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • shortness of breath • itching or rash • dizziness • fever • wheezing • flushing • feeling like passing out 	<p>Rare</p> <p>(less than 1 in 1000 but more than 1 in 10000)</p>

Management of Other Side Effects

SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Allergic reactions to pembrolizumab or bevacizumab may rarely occur. Signs of an allergic reaction may include flushing, rash, itching, dizziness, changes in blood pressure, chest pain, nausea and vomiting, swelling or breathing problems. This can occur immediately or several hours after receiving pembrolizumab or bevacizumab.</p>	<p>Tell your nurse if this happens while you are receiving treatment or contact your oncologist <i>immediately</i> if this happens after you leave the clinic.</p>
<p>Your white blood cells may decrease after your treatment. They usually return to normal after your last 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.</p>	<p>To help prevent infection:</p> <ul style="list-style-type: none"> • Wash your hands often and always after using the bathroom. • Avoid crowds and people who are sick. • Call your healthcare team <i>immediately</i> at the first sign of an infection such as fever (over 38°C or 100°F by an oral thermometer), chills, cough, or burning when you pass urine.

SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Pain or tenderness may occur where the needle was placed.	<ul style="list-style-type: none"> • Apply cool compresses or soak in cool water for 15-20 minutes, several times a day.
Muscle or joint pain may sometimes occur a few days after your treatment	<p>You may take acetaminophen (e.g., TYLENOL®) every 4-6 hours to a maximum of 4 g (4000 mg) per day. Tell your healthcare team if the pain interferes with your activity.</p>
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. • Try the ideas in <i>Fatigue/Tiredness-patient handout*</i>
Hair loss is rare with bevacizumab. If you lose hair, it will grow back once you stop treatment. Colour and texture may change.	<ul style="list-style-type: none"> • If hair loss is a problem, refer to <i>Resources for Hair Loss and Appearance Changes – Patient Handout.*</i>
Loss of appetite and weight loss may sometimes occur, and may persist after discontinuation of treatment.	<ul style="list-style-type: none"> • Try the ideas in <i>Food Ideas to Help with Decreased Appetite.*</i>
Constipation may sometimes occur.	<ul style="list-style-type: none"> • Exercise if you can. • Drink plenty of fluids. • Try the ideas in <i>Food Choices to Manage Constipation.*</i>
Headache may occur.	<ul style="list-style-type: none"> • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours if needed, to a maximum of 4 g (4000 mg) per day.

SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Minor bleeding, such as nosebleeds , may occur.	<ul style="list-style-type: none"> • Sit up straight and tip your head slightly forward. Tilting your head back may cause blood to run down your throat. • Pinch your nostrils shut between your thumb and forefinger or apply firm pressure against the bleeding nostril for 10 full minutes. • After 10 minutes, check to see if your nose is still bleeding. If it is, hold it for 10 more minutes. • Stay quiet for a few hours and do not blow your nose for at least 12 hours after the bleeding has stopped. • Get emergency help if a nosebleed lasts longer than 20 minutes.

***Please ask a member of your healthcare team for a copy.**

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 heartbeat, face swelling or breathing problems.
- Signs of an **infection** such as fever (over 38°C or 100°F by an oral thermometer); chills, cough, pain or burning when you pass urine.
- **Diarrhea** or **changes in bowel habits**; black, tarry stools; blood or mucous in the stool; severe abdominal pain
- Signs of **bleeding problems** such as black, tarry stools, blood in urine, pinpoint red spots on skin, extensive bruising.
- Signs of a **blood clot** such as tenderness or hardness over a vein, calf swelling and tenderness, sudden onset of cough, chest pain, or shortness of breath.
- Signs of **heart or lung problems** such as fast or uneven heartbeat, chest pain, chest pressure, shortness of breath, or difficulty in breathing, swelling of ankles, or fainting.
- Signs of a **stroke** such as sudden onset of severe headache, eyesight changes, slurred speech, loss of coordination, weakness or numbness in arm or leg.
- 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.
- **Seizures** or **fainting**.

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.