

## For the Patient: GICIRB

Other Names: Palliative combination chemotherapy for metastatic cancer of the colon or rectum using irinotecan, bevacizumab and capecitabine

**GI** = GastroIntestinal

**CIRB** = Capecitabine, Irinotecan, Bevacizumab

### ABOUT THIS MEDICATION

#### What are these drugs used for?

- Irinotecan, bevacizumab and capecitabine are drugs given to treat cancer of the colon or rectum.

#### How do these drugs work?

- Irinotecan and capecitabine work by interfering with dividing cells and preventing an increase in the number of cancer cells. Bevacizumab is a monoclonal antibody, which is a type of protein designed to target and interfere with the growth of cancer cells.

### INTENDED BENEFITS

- This therapy is being given to destroy and/or limit the growth of cancer cells in your body. This treatment may improve your current symptoms, and delay the onset of new symptoms.
- It may take a number of treatments before your doctor can judge whether or not this treatment is helping.

### TREATMENT SUMMARY

#### How are these drugs given?

- Irinotecan and bevacizumab are given directly into the vein (IV) and capecitabine is a tablet taken by mouth.
- You will receive irinotecan and bevacizumab at the clinic by a chemotherapy nurse on the first day of treatment **for one day only**. You will be given the capecitabine to start on the same day. Capecitabine is usually given **for 14 days, followed by a 7 day break**. You will take this medication home with you. This 21 day period of time is called a "cycle". The cycle is repeated as long as you are benefiting from treatment and not having too many side effects.
- Each treatment will take **about 2 and a half hours**. Your first treatment will probably take longer, as the nurse will review information on the chemotherapy drug with you.
- Capecitabine will be given to you by a pharmacist when you come in for each irinotecan treatment. You will be given enough tablets so you can take them while at home.

The calendar below shows how the medications are given each 3 week cycle.

C Y C L E	DATE	TREATMENT PLAN
		▶ Week 1 → irinotecan and bevacizumab IV x 1 day → capecitabine orally in a.m.& p.m. x 7 days with food.
	1	Week 2 → capecitabine orally in a.m.& p.m. x 7 days with food.
		Week 3 → No Treatment

The cycles are repeated as long as you are benefiting from treatment and not having too many side effects.

### What will happen when I get my drugs?

- A **blood test** is done each cycle, on or before the first day of each treatment cycle. Your **blood pressure** will be checked by a nurse before each treatment and a **urine test** will be done before each 2<sup>nd</sup> treatment, on even numbered cycles. The dose and timing of your chemotherapy may be changed based on your blood counts 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 drugs in your treatment plan.

Your 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 irinotecan and bevacizumab, and how to manage those side effects with you on the day you receive your first treatment. The pharmacist will review how to take the capecitabine and possible side effects with you on the day you first pick up your medication.

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<b>Allergic reactions</b> may rarely occur. Signs of an allergic reaction are dizziness, feeling faint, confusion, shortness of breath, and wheezing. This may occur immediately or several hours after receiving the drugs. It can occur after the first dose, or after many doses.	Tell your nurse if this happens while you are receiving the drugs or contact your doctor immediately if this happens after you leave the clinic.

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p><b>Nausea and vomiting</b> may occur after your treatment and may last for 24 hours.</p>	<p>You will be given a prescription for anti-nausea drug(s) 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> <p>If nausea is a problem:</p> <ul style="list-style-type: none"> <li>• Sip fluids throughout the day.</li> <li>• Nibble dry starchy foods (toast, cereal, crackers) often.</li> <li>• Try the ideas in <i>Practical Tips to Manage Nausea*</i>.</li> </ul>
<p><b>Early diarrhea</b> may occur very commonly during or shortly after an irinotecan treatment (within 24 hours). It starts with watery eyes, stomach cramps and sweating.</p>	<ul style="list-style-type: none"> <li>• Tell your nurse or doctor immediately if you have watery eyes, stomach cramps or sweating during or after your treatment.</li> <li>• Early diarrhea is treated with a medication called atropine, which is injected into a vein or under your skin. If your cancer centre is closed, your cancer doctor may tell you to go to your Hospital emergency for atropine treatment.</li> </ul>
<p><b>Hand-foot skin reaction</b> may occur very commonly during capecitabine 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.</p>	<ul style="list-style-type: none"> <li>• Avoid tight-fitting shoes or rubbing pressure to hands and feet, such as that caused by heavy activity.</li> <li>• Clean hands and feet with lukewarm water and gently pat to dry; avoid hot water.</li> <li>• Apply lanolin-containing creams (eg. BAG BALM®, UDDERLY SMOOTH®) to hands and feet liberally and often.</li> <li>• Tell your cancer doctor at the next visit if you have any signs of hand-foot skin reaction.</li> <li>• Stop taking capecitabine and call your cancer doctor if the skin reaction is painful, as your dose may need to be changed. Taking a lower dose does not affect the usefulness of capecitabine.</li> </ul>

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p><b>Late diarrhea</b> may occur very commonly one day to several days after an irinotecan treatment. It starts with stools more loose or often than usual.</p> <p>Capecitabine may also cause diarrhea.</p>	<p><b>Late diarrhea must be treated immediately with loperamide 2 mg tablets (e.g. IMODIUM®):</b></p> <ul style="list-style-type: none"> <li>• Take <b><u>TWO tablets</u></b> at the first sign of loose or more frequent stools than usual.</li> <li>• Then take <b><u>ONE tablet every TWO hours</u></b> until diarrhea has stopped for 12 hours.</li> <li>• At night, you may take <b><u>TWO tablets every FOUR hours</u></b> (set your alarm) during the time you usually sleep.</li> <li>• <b>This dose is much higher than the package directions. It is very important that you take this higher dose to stop the diarrhea.</b></li> <li>• Always keep a supply of loperamide (e.g. have 48 tablets on hand). You can buy loperamide at any pharmacy without a prescription.</li> </ul> <p>To help diarrhea:</p> <ul style="list-style-type: none"> <li>• Drink plenty of liquids</li> <li>• Eat and drink often in small amounts</li> <li>• Avoid high fibre foods as outlined in <i>Food Choices to Help Manage Diarrhea*</i>.</li> <li>• A dietician can give you more suggestions for dealing with diarrhea.</li> </ul> <p>If diarrhea does not improve 24 hours after starting loperamide or lasts more than 36 hours, call your doctor.</p>
<p><b>Sore mouth</b> may occur commonly during treatment. Mouth sores can occur on the tongue, the sides of the mouth or in the throat. <b>Mouth sores or bleeding gums can lead to an infection.</b></p>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Make a mouthwash with ½ teaspoon baking soda or salt in 1 cup warm water and rinse several times a day.</li> <li>• Try soft, bland foods like puddings, milkshakes and cream soups.</li> <li>• Avoid spicy, crunchy or acidic food, and very hot or cold foods.</li> <li>• Try ideas in <i>Food Ideas to Try with a Sore Mouth*</i>.</li> </ul>

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Your <b>white blood cells</b> will decrease 1-2 weeks after your treatment. They usually return to normal 3 weeks after your last treatment. White blood cells protect your body by fighting bacteria (germs) that cause infection. When they are low, <b>you are at greater risk of having an infection.</b>	To help prevent infection: <ul style="list-style-type: none"> <li>• Wash your hands often and always after using the bathroom.</li> <li>• Take care of your skin and mouth.</li> <li>• Call your doctor <b>immediately</b> 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.</li> </ul>
Your <b>blood pressure</b> may rise during treatment. This is common.	The chemotherapy nurse will check your blood pressure before each chemotherapy treatment to make sure it is within a range acceptable for treatment. If too high, you may be given medication to lower your blood pressure, or your treatment may be stopped.
<b>Blood clots</b> may rarely occur, usually in the leg. This is more likely to happen if you have had blood clots before. Signs to watch for include tenderness or hardness over a vein, calf tenderness, sudden onset of cough, chest pain, or shortness of breath. Stroke is also a rare event. Signs of a stroke include sudden severe headache, eyesight changes, slurred speech, loss of coordination, and weakness or numbness in arm or leg.	Tell your doctor if you have ever had treatment for a blood clot. To help prevent blood clots: <ul style="list-style-type: none"> <li>• Keep active.</li> <li>• Drink plenty of fluids.</li> <li>• Avoid tight clothing.</li> <li>• Do not sit with your legs crossed at the knees for long periods of time.</li> </ul> If you suspect you are experiencing a blood clot or stroke, see your doctor or seek emergency help immediately.

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<b>Pain or tenderness</b> may occur where the needle was placed.	Apply cool compresses or soak in cool water for 15-20 minutes several times a day.
<b>Constipation</b> may occur.	To help constipation: <ul style="list-style-type: none"> <li>• Exercise if you can.</li> <li>• Drink plenty of fluids (8 cups a day).</li> <li>• Add prunes or prune juice.</li> <li>• Eat foods high in fibre such as bran, whole grain breads and cereals, nuts, fruits and vegetables.</li> <li>• Try ideas in <i>Food Choices to Manage Constipation*</i>.</li> </ul>

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Your platelets may decrease during or after your treatment. They will return to normal after your last treatment. Platelets help to make your blood clot when you hurt yourself. <b>You may bruise or bleed more easily than usual.</b></p>	<p>To help prevent bleeding problems:</p> <ul style="list-style-type: none"> <li>• Try not to bruise, cut, or burn yourself.</li> <li>• Clean your nose by blowing gently. Do not pick your nose.</li> <li>• Avoid constipation.</li> <li>• Brush your teeth gently with a soft toothbrush as your gums may bleed more easily. Maintain good oral hygiene.</li> </ul> <p>Some medications such as ASA (e.g. ASPIRIN®) or ibuprofen (e.g. ADVIL®) may increase your risk of bleeding.</p> <ul style="list-style-type: none"> <li>• Do not stop taking any medication that has been prescribed by your doctor (e.g. <b>ASA for your heart</b>).</li> <li>• For minor pain, try acetaminophen (e.g. TYLENOL®) first, but occasional use of ibuprofen may be acceptable.</li> </ul>
<p><b>Swelling</b> of hands, feet or lower legs is uncommon, but may occur if your body retains extra fluid.</p>	<p>If swelling is a problem:</p> <ul style="list-style-type: none"> <li>• Elevate your feet when sitting.</li> <li>• Avoid tight clothing.</li> </ul>
<p><b>Headaches</b> are uncommon but may occur. These are usually mild.</p>	<ul style="list-style-type: none"> <li>• Take acetaminophen (e.g. TYLENOL®) to decrease or stop the headache.</li> </ul>
<p>Minor bleeding, such as <b>nosebleeds</b>, may commonly occur.</p>	<ul style="list-style-type: none"> <li>• Sit up straight and tip your head slightly forward. Tilting your head back may cause blood to run down your throat.</li> <li>• Pinch your nostrils shut between your thumb and forefinger or apply firm pressure against the bleeding nostril for 10 full minutes.</li> <li>• After 10 minutes, check to see if your nose is still bleeding. If it is, hold it for 10 more minutes.</li> <li>• Stay quiet for a few hours and do not blow your nose for at least 12 hours after the bleeding has stopped.</li> <li>• Get emergency help if a nosebleed lasts longer than 20 minutes.</li> </ul>
<p>You may have <b>trouble sleeping</b> while receiving irinotecan.</p>	<ul style="list-style-type: none"> <li>• Talk to your doctor if your trouble in sleeping continues to bother you.</li> <li>• This will return to normal when you stop treatment with irinotecan.</li> </ul>

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Your <b>skin may sunburn</b> easily.	To help prevent sunburn: <ul style="list-style-type: none"> <li>• Avoid direct sunlight.</li> <li>• Wear a hat, long sleeves and long pants or skirt outside on sunny days.</li> <li>• Apply a sun block lotion with an SPF (sun protection factor) of at least 30.</li> <li>• Refer to Your Medication Sun Sensitivity and Sunscreens* or the BC Health Guide for more information.</li> <li>• After sun exposure, if you have a severe sunburn or skin reaction such as itching, rash, or swelling, contact your doctor.</li> </ul>
Tiredness and lack of energy may occur.	<ul style="list-style-type: none"> <li>• Do not drive a car or operate machinery if you are feeling tired.</li> <li>• Try the ideas in the handout titled <i>Fatigue/Tiredness*</i></li> </ul>
<b>Hair loss is common</b> with irinotecan and may begin within a few days or weeks of treatment. Your hair may thin or you may become totally bald. Your scalp may feel tender. You may lose hair on your face and body. Your hair will grow back once your treatments are over and sometimes between treatments. Colour and texture may changes.	<ul style="list-style-type: none"> <li>• Use a gentle shampoo and soft brush.</li> <li>• Care should be taken with hair spray, bleaches, dyes and perms.</li> <li>• Protect your scalp with a hat, scarf or wig in cold weather. Some extended health plans will pay part of the cost of a wig.</li> <li>• Apply mineral oil to your scalp to reduce itching.</li> <li>• If you lose your eyelashes and eyebrows, protect your eyes from dust and grit with a broad-rimmed hat and glasses.</li> <li>• <a href="#">If hair loss is a problem, refer to Resources for Hair Loss and Appearance Changes*</a>.</li> </ul>

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

### **Special notes:**

**Heart Problems:** Serious heart problems can occur when starting capecitabine. These can rarely be fatal. Problems such as chest pain, heart attack, abnormal heart rhythm, or heart failure can occur. Having a history of heart problems with fluorouracil, a related chemotherapy drug, is a risk factor, as is having a history of prior angina (heart pain) or heart attack. Seek medical attention promptly if you experience feelings of heavy pressure or pain in the chest, trouble breathing, significant worsening leg swelling, or marked lightheadedness. These symptoms can occur within days after starting capecitabine. If your symptoms are severe, you may need to call for emergency help.

**Wound Healing:** Bevacizumab may slow the healing process when recovering from surgery. See the instructions below under “Instructions for Patient” to prevent any problems with wound healing after surgery.

**Bowel Perforation**, a small hole in the wall of part of your intestine, can rarely occur with Bevacizumab. Symptoms may include sudden abdominal pain or tenderness, sometimes with constipation and vomiting.

### **INSTRUCTIONS FOR THE PATIENT**

- Tell your doctor if you have ever had an unusual or **allergic reaction** to fluorouracil (5 FU, ADRUCIL®) before taking capecitabine.
- If you are planning to have **surgery**, bevacizumab may be stopped approximately 4 weeks before surgery and not restarted until approximately 4 weeks after surgery and only if the surgical wound is well healed. This helps to lower the risk of bleeding and may prevent problems with wound healing after surgery.
- The drinking of alcohol (in small amounts) does not appear to affect the safety or usefulness of irinotecan, bevacizumab or capecitabine.
- Irinotecan and capecitabine may damage sperm in males. Irinotecan, bevacizumab and capecitabine may harm the baby if used during pregnancy. It is best to **use birth control** while being treated with these drugs, and for six months after your last treatment. Tell your doctor right away if you or your partner becomes pregnant. Do not breast feed during treatment.
- **Tell** doctors, dentists and other health professionals that you are being treated with irinotecan, bevacizumab and capecitabine before you receive any treatment from them.

### **Capecitabine**

- Capecitabine is taken by mouth twice a day, about 10-12 hours apart, with equal numbers of tablets taken at each dose. You may be given tablets of more than one strength to make the right dose. Capecitabine should be taken within 30 minutes following the end of a meal (breakfast and dinner) with a glass of water. It is usually **given for 14 days, followed by a 7 day break**.
- The tablet contains lactose.
- If you **vomit after taking capecitabine**, do not take a second dose. Call your doctor during office hours for advice.
- If you **miss a dose of capecitabine**, take it as soon as you can if it is within 6 hours of the missed dose. If it is over 6 hours since the missed dose, skip the missed dose and go back to the usual dosing time. Let your doctor know during office hours if you have missed a dose.
- Sometimes capecitabine treatment has to be **stopped for a short time** because of side effects. When you **restart** capecitabine treatment, do not make up for the missed dose; instead, take as directed by your cancer doctor and finish the treatment on the same day as originally planned. For example, if you stop on day 3 of your 14-day treatment course and then restart at a later day, you would still take the last dose on day 14. You may be told to take a different dose and you may have extra tablets left over. Return the extra tablets to the clinic at your next visit. Taking a lower dose does not affect the usefulness of capecitabine.
- **Store** capecitabine tablets out of the reach of children, at room temperature, away from heat, light and moisture.



## Medication Interactions

Some drugs such as warfarin (COUMADIN®), phenytoin (DILANTIN®) and fosphenytoin (CEREBYX®) may **interact with capecitabine**. Other drugs such as laxatives, seizure medicines, St. John's Wort, dexamethasone or prochlorperazine may **interact with irinotecan**.

- Dexamethasone can be taken as an anti-nausea drug. Discuss with your cancer doctor if you are taking dexamethasone on a daily basis.
- Prochlorperazine should not be taken as an anti-nausea drug on the day of your irinotecan treatment.

Tell your doctor if you are taking these or any other drugs as you may need extra blood tests, or your dose may need to be changed. Check with your doctor or pharmacist before you start taking any new drugs.

## THE FOLLOWING INFORMATION IS VERY IMPORTANT

### STOP TAKING CAPECITABINE AND 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); chills; cough; pain or burning when you pass urine.
- 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 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 **bleeding problems** such as black tarry stools; blood in urine; pinpoint red spots on skin, extensive bruising.
- Persistent bleeding, such as **nosebleeds** lasting more than 20 minutes.
- **Diarrhea** that occurs within the first 24 hours after irinotecan treatment.
- Sudden **abdominal pain** or tenderness.
- Signs of **severe fluid loss** due to diarrhea such as fainting, light-headedness or dizziness.
- Severe **headache** that persists, or is associated with vomiting, confusion or visual changes.

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

- **Painful hand-foot skin reaction** such as painful redness, peeling, tingling, numbness, swelling or blistering of the palms of your hands and/or bottoms of your feet. If there is a delay in seeing your doctor, stop taking your capecitabine tablets until you are seen or have discussed with your doctor.
- Severe **diarrhea** that occurs after the first 24 hours and does not improve 24 hours after starting loperamide or lasts more than 36 hours.
- **Nausea** that causes you to eat a lot less than usual or **vomiting** more than 2 times in 24 hours.
- **Painful redness, swelling or sores on your lips, tongue, mouth or throat.**
- Signs of **liver problems** such as yellow eyes or skin, white or clay-colored stools.

- Signs of **anemia** such as unusual tiredness or weakness.
- **Severe abdominal or stomach cramping or pain.**
- Signs of **liver problems** such as yellow eyes, or skin, white or clay-coloured stools.
- Signs of **kidney problems** such as swelling of feet or lower legs.
- **Sores** that do not heal or are slow to heal.
- **Changes in eyesight.**

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

- Painless hand-foot skin reaction such as redness, peeling, tingling, numbness, swelling or blistering of the palms of your hands and/or bottoms of your feet,
- Painless redness, swelling or sores on your lips, tongue, mouth or throat.
- Uncontrolled nausea, vomiting, loss of appetite, diarrhea or constipation.
- Skin rash or itching.
- Changes in fingernails or toenails.
- Heartburn; mild to moderate abdominal or stomach pain.
- Easy bruising or minor bleeding
- Redness, swelling, pain or sores where the needle was placed.
- Watery, irritated eyes.
- Trouble sleeping.
- Skin rash or itching.

**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: \_\_\_\_\_