

Regorafenib

Stivarga®

Cancer-directed targeted therapy in tablets

Understanding your treatment

What is targeted therapy?

This treatment targets specific molecules, which are inside or on the surface of cancer cells. By targeting cancer cells, the targeted therapy limits damage to healthy cells. This type of treatment can be used alone or in combination with other treatments such as chemotherapy.

How can a targeted therapy help you?

Depending on your type of cancer and the stage of the disease, a targeted therapy can be used to :

- **Destroy** cancer cells
- **Stop** the cancer from spreading
- **Slow** the growth of cancer cells

How will you feel while on a targeted therapy?

Even though those treatments target cancer cells and limit damage to healthy cells, side effects can still arise.

Not everyone has side effects and each person's experience may differ. Side effects and their severity are not representative of the treatment's effect or lack thereof.

This document presents the most frequent side effects that your targeted therapy causes.

Medication

Regorafenib

Tablets to take by mouth

Administration

Tablets to be taken once daily for 3 weeks, followed by 1 week off.

Total daily dose : ____ 40 mg tablets

To be taken with a light, low-fat and low-calorie meal (300 to 550 calories) – see last page for meal examples.

Cycle repeated every 4 weeks (3 weeks of treatment followed by 1 week off)



A **blood test** will be done throughout your treatment. Depending on the results and side effects of the previous treatment, the dose of the medication might be adjusted or the treatment might be delayed.

How to take your medication?

- Take your regorafenib tablets, as prescribed once a day, at the same time everyday. Take your tablets with a light, low-fat and low-calorie meal (see last page for meal examples).
- Tablets must be taken whole. Do not chew, split or crush the tablets.
- **If you forget a dose**, you may take it as soon as you remember if less than 12 hours have passed since the missed dose. Do not double your next dose. Try, however, to take your tablets at the same time every day and in the same way (with a light meal).

Storing and handling your medicines



- Wash your hands immediately after handling your tablets.
- Keep your medication at room temperature, out of the reach of children and pets as well as protected from light, heat or moisture. Do not keep medicines in the bathroom.
- Don't throw away unused medication at home. Bring it back to your pharmacy to be destroyed safely. You may dispose of the empty containers in your home garbage can.
- Pour the pills from the container into the cap to avoid contact with other surfaces. If it inadvertently comes in contact with the surrounding surface, wash and rub the surface with water and soap.
- Caregivers should wear disposable gloves if they prepare medication for you. You can find disposable gloves at your local community pharmacy.
- Keep your medications in their original container and do not mix them with other drugs. The container should never be reused to put other objects or food.

How can this treatment affect your daily life?

Appetite

- Your **appetite may diminish**. Eat more often, in smaller quantities.
- Your **sense of taste may be altered**. Enhance foods with *fines herbes* or lemon juice. Eating fruits and unsweetened candies, chewing non-sugared gums, etc., may mask the metallic taste.
- **Alcohol** in small quantities is allowed and will not affect the efficacy of the treatments.

Sex life and birth control

- You can have an **active sexual** life during your treatments. However, a decrease in your sexual drive may occur during this period. This may also be influenced by different factors (fatigue, stress, etc.).



- It's safe to kiss, to touch, to hold hands, to sleep in the same bed and to cuddle.
- The effect of the drug on male or female fertility is unknown. This medication may have an effect on the menstrual cycle as well as spermatozoid production. However, this does not prevent erection or sexual activity and as such, you can have an active sexual life during your treatments. Pregnancy is possible and this medication could be harmful to the fetus. The use of an effective method of contraception is highly recommended for both men and women while on treatment and up to 8 weeks after the end of the treatment. Breast-feeding is contraindicated during treatment.

Foods and medicines to avoid



- **Grapefruit**
You must avoid consuming grapefruit, Seville orange, starfruit, pomelo, pomegranate or foods containing them. The consumption of those foods could increase the side effects of regorafenib.

Tips and precautions



- **Sit down to urinate and fold down the toilet lid**
Women as well as men should sit down to urinate and fold down the toilet lid before flushing in order to avoid splashing. Flush twice to make sure everything has been flushed away. Follow these precautions during your treatments and up to 48 hours after (or according to instructions from your cancer center).
- **Bodily fluids**
The treatment you're receiving stays in your body for a few days. During that period, it's possible that a certain quantity is found in some bodily fluids or secretions that you produce, such as urine, stools, vomit, sperm and vaginal discharge. In order to protect the environment and those living with you, follow the instructions given by your cancer center about the right way to handle and dispose of the bodily fluids.



- **Over the counter medicines, natural health products and vaccines**
Consult your healthcare team :
 - if you intend to take any other medication (with or without a prescription) or natural health products.
 - if you need to receive a vaccine.
 This could decrease your treatment's efficacy or increase its side effects.
- **Always have on hand the complete list of your medications**
Be sure to always have on hand the complete list of your medications, dietary supplements, vitamins and other natural health products. Give it to you doctor and your pharmacist. It is important to make them aware of any change.
- Notify your dentist or physician that you are taking regorafenib if you have to undergo surgery while on treatment.



What are the side effects of your treatment?

This fact sheet aims to let you know the side effects most commonly seen following the administration of your treatment. Please note that when you take any medication, there is a possibility that it causes rare side effects and it is difficult to predict which patients will be affected.

ADVERSE EFFECTS

MANAGEMENT

Fatigue

Significant fatigue and weakness may occur during your treatments. It is usually temporary and may be related to many factors (medication, stress, disease...).

- Maintain a good level of activity but take some rest when you feel tired.

Hand and foot problems

Hand and foot syndrome may appear during your treatment. You may experience numbness, tingling, swelling, redness on the palms your hands and underneath your feet. Pain, blisters, peeling of the skin may accompany these symptoms.

To prevent this syndrome :

- Avoid wearing tight clothes or shoes. Wear absorbent sponge rubber soles, and/or gel pads to relieve pressure points.
- Pat dry your hands and feet rather than rubbing them.
- Wear light clothing or keep skin free of clothing to avoid perspiring.
- Wear rubber gloves while washing dishes.
- Wash your hands and feet in lukewarm water; avoid hot water.
- Moisturize your skin regularly using a non-perfumed emollient and thick cream.
- Avoid activities that require applying pressure and repetitive friction on your hands and feet.

If symptoms occur :

- ✓ **Continue your treatment but contact your healthcare team if:** you have numbness, redness, or tingling on your hands and feet, but it's not painful.
- ⚠ **Stop your treatment and call your healthcare team as soon as possible if:** you have redness, swelling or peeling of the skin with pain to the hands and feet, but it does not prevent you from doing your daily activities.
- ✗ **Stop your treatment and call your healthcare team as quickly as possible or go to the Emergency Room if:** you have redness, swelling and lesions (ulcers) to the hands and feet with pain, and if it prevents you from doing your daily activities.



ADVERSE EFFECTS

MANAGEMENT

Diarrhea

You may sometimes experience diarrhea.

- Drink lots of liquids (8 to 10 glasses a day) unless otherwise instructed by your doctor.
- Eat and drink often but in small quantities.
- ✓ **Continue your treatment if:** you have light diarrhea (2 to 3 additional loose stools per day compared to usual before starting your treatment). Start loperamide (Imodium®) by taking 2 tablets first followed by one tablet after each loose stool for a maximum of 8 tablets per 24 hours period. Contact a member of your healthcare team if the diarrhea does not improve after taking loperamide for 24 hours.
- ⚠ **Continue your treatment and call your healthcare team as soon as possible if:** you experience more than 4 to 6 additional loose stools per day compared to usual before starting your treatment. Start loperamide (Imodium®) by taking 2 tablets first followed by one tablet after each loose stool for a maximum of 8 tablets per 24 hours period.
- ✗ **Stop your treatment and call your healthcare team as quickly as possible or go to the Emergency Room if:** you have 7 or more additional loose stools per day compared to usual before starting your treatment, if you are not able to hold it in (incontinence) or if you have diarrhea with a fever.

Voice changes

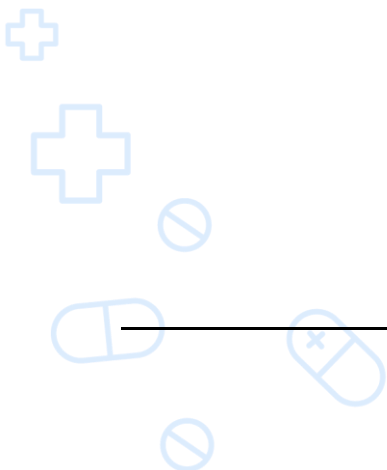
A voice change (most commonly hoarseness) may happen during your treatment.

- If it bothers you, contact a member of your healthcare team.

High blood pressure

High blood pressure might occur.

- Your blood pressure might be checked during your visit with your doctor.
- A member of your healthcare team might ask you to measure your blood pressure regularly and record it in a diary.
- If you experience high blood pressure, medication can be prescribed to control it.
- ✓ **Continue your treatment if:** your resting blood pressure is below 140/90 mmHg.
- ⚠ **Continue your treatment and call your healthcare team as soon as possible if:** your blood pressure is above 140/90 mmHg over a short period of time or less than 24 hours.



- ➖ **Stop your treatment and call your healthcare team as quickly as possible if:** your blood pressure is above 160/100 mmHg all or most of the time. **Head to the Emergency Room** if your blood pressure is above 200/120 mmHg or if you have a headache or are confused.

Ulcers in the mouth

Ulcers in the mouth and the throat may appear during your treatment. These ulcers can also appear in the throat.

- Gently and regularly brush your teeth after each meal and at bedtime.
- To prevent this effect, rinse your mouth with a solution of water and salt with or without baking soda or mouthwashes **without** alcohol found in stores. Gargle 4 times a day – after every meal and at bedtime. Do not drink or eat for one hour after you gargle.
- ✓ **Continue your treatment if:** you have mild discomfort (ulcer, sensitivity, redness, irritation) that does not prevent you from eating. Continue your mouthwash.
- ⚠ **Stop your treatment and call your healthcare team as soon as possible if:** you have moderate discomfort (redness and painful lesions) that prevents you from eating, but not completely. Continue your mouthwash.
- ➖ **Stop your treatment and call your healthcare team as quickly as possible or go to the Emergency Room if:** you have severe discomfort and pain that is bothersome enough that it prevents you almost completely from eating.

Skin problems

You might experience some **skin reactions** within about 1 or 2 weeks of starting your treatment. These reactions usually present with :

- A **rash** on the face, neck, chest, back, and arms. This reaction looks like acne and usually disappears within a few weeks after the end of the treatment.
- Your **skin** may become **drier**. **Redness** and **itchiness** may develop.
- Your skin may become more **sensitive to the sun**.

To help prevent or decrease these reactions :

- Use fragrance-free, alcohol-free mild soap or cleaning products. Also use bath or shower oils to avoid skin dryness.
- Moisturize your skin twice a day with fragrance-free, thick, emollient-based creams like Aveeno®, Neutrogena® or Vaseline Intensive Care® lotion.
- Use non-perfumed creams and cosmetics without alcohol or dye. Use dermatologist-recommended make up (foundation) to mask skin problems.
- Remove make up with a mild cleaning product.
- Avoid sun exposure. In case of unavoidable sun exposure, wear a hat and clothes with long sleeves.
- Avoid over-the-counter acne products as they can dry skin.
- Use a broad-spectrum sunscreen (SPF of 30 or more).

If despite all these measures, skin reactions appear:

Nausea

Rarely, slight nausea may occur during your treatment.

- Consult a member of your healthcare team who will recommend appropriate measures.

- You will be prescribed medication to be taken as needed if you have nausea.

✔ **Continue your treatment if:** you have light nausea that does not prevent you entirely from eating. Make sure to continue your medication prescribed for your nausea.

⚠ **Continue your treatment and call your healthcare team as soon as possible if:** you have significant nausea, experience vomiting that is partially preventing you from eating. Make sure to continue your medication prescribed for your nausea.

⊖ **Stop your treatment and call your healthcare team as quickly as possible or go to the Emergency Room if:** you have severe nausea or repeated vomiting that prevents you completely from eating.

Decrease in platelets

A decrease in **platelets** may occur during your treatment. You may bruise or bleed more easily than you normally do.

- Use a tooth brush with soft bristles.
- Consult your pharmacist before taking over the counter medications containing Aspirin® or other anti-inflammatory medication (e.g. Advil®, Motrin®, Aleve®, etc.).
- Contact a member of your healthcare team if you bruise more easily than you normally do or if you have a tendency to bleed easily from the nose or the gums.

Decrease in white blood cells

A decrease in the **white blood cells** is unlikely during your treatment. Nevertheless, you could be at higher risk to contract infections during this period.

- Wash your hands often.
- During this period, avoid coming in contact with people who have contagious diseases.
- Contact a member of your healthcare team quickly if you notice any signs of infection (chills, cough, sore throat, pain while you urinate, etc.)
- In case of fever, do not take acetaminophen (Ex : Tylenol®, Atasol®) and anti-inflammatory medication (Ex : Motrin®, Advil®, Aleve®).
- ⊖ **Stop your treatment and go the Emergency Room if :**
 - you have a fever of 38,3°C (101°F) or above
 - or
 - you have a fever of 38°C (100,4°F) twice an hour apart.



ADVERSE EFFECTS

MANAGEMENT

Hair loss

Depending on the individual, **thinning of the hair** may occur. However, don't worry; your hair will grow back after treatments have ended.

- Use gentle shampoo.
- In order to slow hair loss, avoid brushing hair vigorously.
- Avoid hair spray, dyes and perms.

RARE ADVERSE EFFECTS THAT CAN BE SEVERE OR SERIOUS

If the following side effects occur, stop your treatment and call your healthcare team as quickly as possible or go to the Emergency Room:

- Severe headache, visual problems, difficulty talking, loss of coordination, weakness or dizziness, chest pain or chest tightness.

PHARMACIST : _____

PHONE : _____

FROM ____ H ____ TO ____ H ____ (MONDAY TO FRIDAY)

This fact sheet has been prepared by a sub-committee of the Comité national de l'évolution de la pratique des soins pharmaceutiques of the Programme québécois de cancérologie of the Ministry of Health and Social Services in consultation with the Comité de l'évolution de la pratique en oncologie of the Institut national d'excellence en santé et en services sociaux.

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EXAMPLES OF LOW-FAT AND LOW-CALORIE MEALS

Breakfast

125 mL (½ cup)	Orange juice
175 mL (¾ cup)	Instant oatmeal
or	
250 mL (1 cup)	Breakfast cold cereals, minimally processed (Corn Flakes, Rice Krispies, Spécial K, Cheerios, etc.)
250 mL (1 cup)	Partly skimmed milk, 2% m.f.
1	Medium banana
250 mL (1 cup)	Coffee
10 mL (2 teaspoons)	Sugar
Total	~475 kcal, 8 g of lipids (15%)

1	Medium orange
2 slices	Whole wheat bread, toasts
1	Large fried egg
15 mL (1 tablespoon)	Jam
250 mL (1 cup)	Coffee
30 mL (2 tablespoons)	Partly skimmed milk, 2% m.f.
Total	~415kcal, 9 g of lipids (20%)

Dinner or supper

75 g	Chicken breast, roasted
or	
75 g	White fish, roasted
125 mL (½ cup)	Converted long grain rice, cooked
125 mL (½ cup)	Cooked vegetables (carrots, broccoli, etc.)
100 g	Fruit yogurt, 2% m.f.
125 mL (½ cup)	Fresh strawberries
2	«Social Tea» type cookies
250 mL (1 cup)	Tea
Total	~440 kcal, 7 g of lipids (14%)

1	Low-fat, frozen dinner
1	Chocolate chip chewy granola bar
250 mL (1 cup)	Skimmed milk, 0% m.f.
Total	Entre 400 à 500 kcal, 7 à 12 g of lipids (16 à 22%)

1	Roastbeef sandwich (with mustard, lettuce, tomato and 1 slice of cheddar cheese)
250 mL (1 cup)	Mixed lettuce, mixed green salad mix
15 mL (1 tablespoon)	Low-fat dressing
1 box	Fruit juice
Total	495 kcal, 14.5 g of lipids (26%)







Treatment Diary | Regorafenib




CYCLE START DATE :

LEGEND (Refer to the information sheet for more details.)

- ✓ Continue your treatment.
- ⚠ **Stop** your treatment and contact your healthcare team as soon as possible (**hand and foot problems, ulcers in the mouth**).
- ⚠ **Continue** your treatment and contact your healthcare team as soon as possible (**diarrhea, high blood pressure, nausea**).
- ⊘ Stop your treatment and contact your healthcare team without delay or go to the Emergency Room.

		TREATMENT																				REST							
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
(Record the number of tablets taken)		mg																											
Date (dd-mm)																													
HAND AND FOOT PROBLEMS		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
✓	Numbness, redness, or tingling on your hands and feet, but it's not painful.																												
⚠	Redness, swelling or peeling of the skin with pain to the hands and feet, but it does not prevent you from doing your daily activities.																												
⊘	Redness, swelling and lesions (ulcers) to the hands and feet with pain, and if it prevents you from doing your daily activities.																												
DIARRHEA		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
✓	Light diarrhea: you have 2 to 3 additional loose stools per day compared to usual.																												
⚠	Moderate diarrhea : you have 4 to 6 additional loose stools per day compared to usual.																												

	Severe diarrhea : you have 7 or more additional loose stools per day compared to usual before starting your treatment or you are not able to hold it in (incontinence).																													
HIGH BLOOD PRESSURE		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
	Resting blood pressure below 140/90 mmHg.																													
	Blood pressure above 140/90 mmHg over a short period of time or less than 24 hours.																													
	Blood pressure above 160/100 mmHg all or most of the time over a period of 24 hours.																													
ULCERS IN THE MOUTH		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
	Mild discomfort (ulcer, sensitivity, redness, irritation) that does not prevent you from eating.																													
	Moderate discomfort (redness and painful lesions) that prevents you from eating, but not completely.																													
	Severe discomfort and pain that is bothersome enough that it prevents you almost completely from eating.																													

NAUSEA AND VOMITING		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
	Light nausea that does not prevent you entirely from eating.																												
	Significant nausea or if you experience vomiting that is partially preventing you from eating.																												
	Severe nausea or repeated vomiting that prevents you completely from eating.																												