

HOW TO TAKE YOUR MEDICATION:

- Zelboraf is taken by mouth twice a day. Your dose is _____ tablets at a time.
- Cotellic is also taken by mouth, once a day. Your dose is _____ tablets at a time.
- You **DO NOT** take Cotellic the last 7 days of each 28-day cycle. (See the attached calendar for more information.)
- Both drugs can be taken with food or without food.
- The doses of the drugs may be lowered by your oncology team if you have a lot of side effects or other problems.

WHAT TO DO IF YOU MISS A DOSE:

- If you miss taking your Zelboraf dose and it is less than 4 hours until your next dose, **DON'T TAKE** the missed pills. If it is more than 4 hours until your next dose, take the dose.
- If you miss taking your Cotellic by more than 4 hours from the scheduled time, **DON'T TAKE** the missed pills. If it is within 4 hours of the scheduled time, take the dose.

Ways that can help you remember to take your pills: You can use the attached calendar, checking off each dose you take. You could also use a smartphone alarm, or put reminders on mirrors, doors, or your laptop. You can decide what works best for you.

Be sure to bring your calendar to your visits with your oncology team.

If you or your partner becomes pregnant: Tell your oncology team right away if you or your partner becomes pregnant or think you are pregnant while on these medications as they can harm a developing fetus. Be sure to use effective birth control if you are a woman of child-bearing age or a man who is sexually active.

Common side effects of this combination therapy:

Even small side effects could be serious and you should report ALL of them to your oncologist's office. The most common side effects of taking Cotellic/Zelboraf are...

- Diarrhea
- Fatigue
- Skin rash
- Nausea
- Vomiting
- Fever
- Joint aches and pains
- A skin reaction to sunlight

SIGNS OF AN ALLERGIC REACTION TO THE MEDICATIONS:

Stop taking your medications and get medical help immediately if you have any of these signs of a serious allergic reaction:

- A rash or redness all over your body
- Trouble breathing or swallowing
- Swelling of the face, lips, or tongue
- Tightness in the throat or a hoarse voice
- Feeling faint
- A fast heartbeat.

You may want to keep a notebook as your treatment diary and write down when you take your pills, how many pills you take, and if you have any side effects.

Be sure to bring this treatment diary to your visits with your oncology team.

IMPORTANT SIDE EFFECTS

Your oncology team may discuss some side effects of Cotellic/Zelboraf that can lead to serious problems if they aren't taken care of right away. These sections give information about possible symptoms, what you should tell your oncology team, when you should get medical help immediately, and any steps you can take to help ease the symptoms.

FEVER, WITH OR WITHOUT CHILLS

COTELLIC® (cobimetinib)/ZELBORAF® (vemurafenib)
Combination for Melanoma

Report immediately to your oncologist's office

What are the symptoms?

Temperature of _____°F or higher or chills without a fever

What you should tell your oncology team member:

- What your temperature reading is.
- When the fever started and how long it has lasted.
- What type of thermometer you used to take your temperature.
- If you have chills, stomach or breathing problems, feel dizzy when you stand up quickly, feel very tired, and/or have not been going to the bathroom (urinating) as much as you usually do.
- How much and what you have been drinking over the past 24 hours.
- If you have recently been around people with colds/flu or animals, or if you have traveled nationally or internationally.

Red flags – Call your oncologist's office immediately – if they are not available, go directly to the Emergency Room.

- A fever over 104.0°F.
- Any fever and passing out or feeling faint.

Managing Your Side Effects

- If approved by your oncologist's office, take over-the-counter pain relievers such as acetaminophen (Tylenol®) or ibuprofen (Advil®, Motrin®) every 6 hours until the fever goes away. Don't take more than 3000 mg a day of acetaminophen or 2400 mg a day of ibuprofen.
- Take a cool or slightly warm bath.
- Put cool compresses or a cold pack on your forehead and neck.
- Drink water and other liquids such as juice and sports drinks (Gatorade®, Powerade®, and Pedialyte®) or suck on popsicles to prevent dehydration.

SKIN CHANGES

COTELLIC® (cobimetinib)/ZELBORAF® (vemurafenib)
Combination for Melanoma

Report immediately to your oncologist's office

What are the symptoms?

- A reddish bump that bleeds or doesn't heal
- Changes in the size or color of a mole
- Redness of the skin that looks like a sunburn
- Itching
- A rash
- A new wart
- A skin sore

What you should tell your oncology team member:

- When you first noticed the skin change or itching.
- What the “rash” looks like – (eg, flat, bumpy, acne-like, etc.).
- Where and how much of your body the rash covers.
- If the skin change is making it difficult for you to get dressed, eat, or sleep.
- If you have had any skin problems in the past.
- If you have been using a new soap or been around new chemicals or animals recently.
- What the rash looks like (eg, does it look like acne, hives).

Red flags – Call your oncologist's office immediately – if they are not available, go directly to the Emergency Room.

- A rash that covers a large part of your body or that is quickly getting worse.
- Blisters (on your skin or in your mouth) that are peeling. Skin that looks infected (red streaks, pus, or draining).
- Any rash that is accompanied by a fever.

Managing Your Side Effects

- Avoid soap. Instead, use gentle, non-soap cleansers such as Cetaphil®.
- Avoid hot baths.
- Avoid tight clothing and shoes.
- Keep your fingernails short to stop yourself from scratching.
- Apply a moisturizer daily.
- Protect your skin from the sun by wearing sunscreen (30 SPF or higher), a hat, and UV-protective clothing and sunglasses. Don't forget your hands and face.
- Your oncology team may tell you to take an antihistamine or pain reliever to reduce the pain and itching.
- Have regular skin exams before and during treatment.

EYE AND VISION PROBLEMS

COTELLIC[®] (cobimetinib)/ZELBORAF[®] (vemurafenib)

Combination for Melanoma

Report immediately to your oncologist's office

What are the symptoms?

- Eye pain, swelling, or redness
- Partial or full loss of vision
- Blurred vision
- Seeing halos or other vision problems

What you should tell your oncology team member:

- When you started to have vision problems, how severe they are, and how long they have lasted.
- If you have had any vision problems in the past, such as dry eyes or glaucoma.
- If you recently have had an eye injury, started on a new medication, or been exposed to chemicals.
- If you wear contact lenses.
- If you have diabetes.
- If you have any other symptoms, such as a headache, vomiting, or nausea.
- When you last had an eye examination.

Red flags – Call your oncologist's office immediately – if they are not available, go directly to the Emergency Room.

- Sudden and severe symptoms, such as sudden vision changes, eye pain, redness, or unusual sensitivity to sunlight and glare.

Managing Your Side Effects

- Follow your oncology team's instructions for getting eye exams at the eye doctor.
- Wear sunglasses to protect your eyes from the sun's damaging rays.
- If you wear contact lenses, be careful to follow guidelines for keeping your eyes hydrated well and for cleaning, wetting, and replacing lenses.
- If you have diabetes, keep your blood glucose level under good control to reduce the risk of eye disease.
- Follow a healthy lifestyle to take care of your eyes as well as your body.

POTENTIAL HEART PROBLEMS

COTELLIC® (cobimetinib)/ZELBORAF® (vemurafenib)

Combination for Melanoma

Report immediately to your oncologist's office

What are the symptoms?

- Chest pain
- Changes in energy level or shortness of breath while resting or when active
- Frequent coughing or wheezing (making a whistling sound while breathing)
- Swelling in the legs or ankles
- Feeling that your heart is skipping a beat, fluttering, or beating too hard or too fast
- Dizziness
- Fainting
- Excessive sweating

What you should tell your oncology team member:

- When you started to have any of these symptoms, how severe they are, and how long they have lasted.
- If you had any of these symptoms before you started Cotellic/Zelboraf.
- If you have been told in the past that you have a heart condition.

Red flags – Call your oncologist's office immediately – if they are not available, go directly to the Emergency Room.

- Sudden onset of these symptoms.
- Any chest pain.
- Difficulty breathing.
- Fainting.

Managing Your Side Effects

- Follow your oncology team's instructions for tests on your heart.
- Be sure to drink enough liquids to stay hydrated.
- Avoid drinking alcohol or taking drugs that affect the heart or brain (such as marijuana, sleeping pills, or stimulants) unless told to do so by your healthcare providers.
- Follow a healthy lifestyle to take care of your heart as well as your body.
- If you are on any medications for your blood pressure or your heart, be sure to take them as ordered and not miss any doses.

JOINT PAIN, SWELLING, OR STIFFNESS

COTELLIC[®] (cobimetinib)/ZELBORAF[®] (vemurafenib)
Combination for Melanoma

Report immediately to your oncologist's office

What are the symptoms?

Joint pain, swelling, and/or stiffness

What you should tell your oncology team member:

- When these symptoms started, what causes them, and how long they lasted.
 - Which joints are affected.
 - If you have ever had any joint problems in the past.
-

Red flags – Call your oncologist's office immediately – if they are not available, go directly to the Emergency Room.

- Sudden or severe onset of joint pain, swelling, or stiffness.
 - If the joint looks deformed.
 - If you can't place weight on the joint (such as your ankle) or use it at all.
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Managing Your Side Effects

- With the approval of your oncologist's office, take anti-inflammatories/pain relievers such as aspirin, ibuprofen (Advil[®], Motrin[®]), or naproxen (Aleve[®]) to relieve pain and stiffness. Ask your oncology team member about how much to take.
- Apply an ice pack to swollen joints for 15 minutes several times a day.
- Keep the joint above your heart whenever you can to reduce swelling.
- Use elastic wrap or tape on the joint to support it.
- Avoid activities that cause pain, but try to maintain some exercise routine, if possible.

OTHER SYMPTOMS TO LOOK OUT FOR

Below are other symptoms you may experience when taking Cotellic®/Zelboraf®. We are very concerned about symptoms we have marked with a check mark. Please call the office if you develop any of these symptoms. Call your oncologist's office immediately if you develop any of the red-flag symptoms. If they aren't available immediately, go to the Emergency Room.

✓	Symptoms	Red flags (Signs that something serious is going on that needs immediate attention)
	Bowel movement changes or constipation (infrequent bowel movements)	If your stools are black or red plus you have pain and fever
	Bruising (black and blue marks)	—
	Chills (shaking) or feeling cold when you don't have a fever	—
	Diarrhea (loose or frequent stools)	Severe pain in the stomach; stools that are bloody or that look like tar
	Dizziness (lightheadedness)	If you faint
	Fatigue (feeling weak or tired)	If you faint
	Headaches	If you have a very painful headache (the "worst headache of your life"), head pain that doesn't go away after a few hours, or head pain with fever, neck pain or stiffness, and/or rash
	Muscle aches, pains, spasms, or weakness	If these symptoms occur along with dark, reddish urine
	Nausea (upset stomach)	If you have any uncontrolled nausea that is keeping you from eating and/or drinking
	Reactions to the sun (severe sunburn; red, painful, dry itchy skin that is hot to the touch; sun rash; skin irritation; bumps; thickened, dry, wrinkled skin)	If you have redness all over your body, blisters on your skin or in your mouth, and/or your skin peels
	Shortness of breath (trouble breathing)	<ul style="list-style-type: none"> • If you have any trouble breathing at rest • If you have shortness of breath and chest pain and/or fainting
	Skin inflammation (swelling) in areas treated with radiation	—
	Stomach pain	If you have sudden severe pain or tenderness in the stomach, blood in the stool, you're vomiting blood, and/or your skin or eyes are turning yellow
	Swelling in your arms or legs	If you have a warm, tender spot on your leg that doesn't get cooler when you put ice on it, and/or if the spot is itchy or tingles, and/or the pain gets worse for no reason
	Thirst, more than usual	If you have great thirst along with feeling very tired, a lack of sweating on a hot day, weakness, dizziness, nausea

OTHER SYMPTOMS TO LOOK OUT FOR

(Continued)

✓	Symptoms	Red flags (Signs that something serious is going on that needs immediate attention)
	Urine, dark or reddish	If you have bright red blood in your urine. If at the same time, if you also feel dizzy, have pain in the back or side, a taste like metal in your mouth, feel sick to your stomach, are vomiting, feel very tired, have shortness of breath, and/or swelling of arm, legs, or the face
	Urination, less than usual	If you also have blood in the urine, swelling of the ankles, and don't feel like eating
	Urination, more than usual	—
	Vaginal bleeding	If you are bleeding for many hours or bleeding a lot (more than one pad an hour) and have severe stomach pain
	Vomiting (throwing up)	If you go more than 24 hours without being able to hold down foods or liquids, and/or you vomit blood or you have severe stomach pain
	Vomiting (throwing up) blood	If you throw up any blood
	Weakness	<ul style="list-style-type: none"> • If weakness is on the face or one side of body plus you have numbness, slurred speech, confusion, drooping in the face • If weakness is all over the body and you feel very tired and even faint, have a fever, or your heart is racing



RESOURCES

Financial Assistance

- Cotellic and Zelboraf Access Solutions
888-249-4918
<http://www.genentech-access.com/cotellic/patients>

COTELLIC[®] (cobimetinib)/ZELBORAF[®] (vemurafenib) Patient Resources

For more information about this therapy and support:

- Nursing Hotline
855-MY-COTELLIC (855-692-6835)

Additional Information Resources

- AIM at Melanoma Foundation (Nurse On Call, patient symposia, drug resources, etc)
AIMatMelanoma.org
- American Cancer Society: Targeted therapy for melanoma skin cancer
<https://www.cancer.org/cancer/melanoma-skin-cancer/treating/targeted-therapy.html>

Cotellic/Zelboraf Dosing Calendar

START DATE: _____

WEEK 1	WEEK 2	WEEK 3	WEEK 4
<div style="display: flex; justify-content: space-between;"> <div> <p>_____ day</p> <p>Date: _____</p> </div> </div>	<div style="display: flex; justify-content: space-between;"> <div> <p>_____ day</p> <p>Date: _____</p> </div> </div>	<div style="display: flex; justify-content: space-between;"> <div> <p>_____ day</p> <p>Date: _____</p> </div> </div>	<div style="display: flex; justify-content: space-between;"> <div> <p>_____ day</p> <p>Date: _____</p> </div> </div>
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NO COTELLIC THIS WEEK			

For a missed dose of Cotellic: If 4 hours or less from scheduled dosing time, take the dose; more than 4 hours, hold that dose and take the next scheduled dose at the normal time.
 A missed dose of Zelboraf can be taken up to 4 hours prior to the next dose.
 Do not take a double dose to make up for a missed dose.

For more information see Genentech USA, Inc. (2016). Cotellic® (cobimetinib) [Package Insert]. Retrieved from: https://www.gene.com/download/pdf/cotellic_prescribing.pdf.
 Also see supplemental materials from Latkin, J., Ascierto, P. A., Dreno, B., Atkinson, V., Liszkay, G., Maio, M., . . . Ribas, A. (2014). *New England Journal of Medicine*, 371, 1867–1876.

For more information see Genentech USA, Inc. (2016). Zelboraf® (vemurafenib) [Package Insert]. Retrieved from https://www.gene.com/download/pdf/zelboraf_prescribing.pdf.

