

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

COTELLIC® cobimetinib tablets

Read this carefully before you start taking COTELLIC and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional (doctor, pharmacist or nurse) about your medical condition and treatment and ask if there is any new information about COTELLIC.

Serious Warnings and Precautions

Side effects of COTELLIC in combination with ZELBORAF® (vemurafenib), which have sometimes been serious or life-threatening, include:

- **Heart problems that can lead to inadequate pumping of the blood by your heart**
- **Bleeding problems, including bleeding in a critical area or organ of your body**
- **Eye problems**

COTELLIC should not be used with certain types of drugs that can increase the blood level of COTELLIC.

COTELLIC in combination with ZELBORAF should be prescribed and managed by a doctor who knows how to use anti-cancer drugs.

What is COTELLIC used for?

COTELLIC is used to treat adult patients with a type of skin cancer called melanoma that has spread to other parts of the body or cannot be removed by surgery.

- It is used in combination with another anti-cancer medicine called ZELBORAF. You should also read the patient medication information leaflet that comes with ZELBORAF.
- It can only be used in patients whose cancer has a specific type of change (mutation) in a gene called “BRAF”. You should have your cancer tested for this change in the “BRAF” gene before starting treatment with COTELLIC in combination with ZELBORAF.

How does COTELLIC work?

COTELLIC targets a protein called “MEK” that is important in controlling cancer cell growth. When COTELLIC is used in combination with ZELBORAF (which targets proteins made from the changed “BRAF” gene), it further slows down or stops the growth of your cancer.

What are the ingredients in COTELLIC?

Medicinal ingredients: cobimetinib fumarate

Non-medicinal ingredients: croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol 3350 (macrogol 3350), polyvinyl alcohol, talc, and titanium dioxide.

COTELLIC comes in the following dosage forms:

Tablets, 20 mg

Do not use COTELLIC if:

- You are allergic to cobimetinib or any of the other ingredients in COTELLIC

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take COTELLIC. Talk about any health conditions or problems you may have, including if you:

- have melanoma cancer in your brain that has not been treated
- have any heart problems
- have high blood pressure (hypertension)
- have any health conditions or take any medicines that may increase your risk of bleeding, such as blood thinners (e.g. warfarin) and medicines that may affect blood clotting (e.g. clopidogrel, aspirin, naproxen and ibuprofen)
- have any liver problems
- have any allergies to medications
- have any muscle problems
- have any eye problems or related risk factors such as high cholesterol levels, for serious eye problems that may occur with COTELLIC
- are planning to have a child in the future. COTELLIC may reduce your fertility.
- have any previous or current skin problems, including skin cancers other than melanoma
- have high blood sugar levels (diabetes)
- have any other medical conditions
- are pregnant, think you may be pregnant, or plan on becoming pregnant. COTELLIC can harm your unborn baby.
 - Female patients who take COTELLIC should use two forms of birth control during treatment with COTELLIC and for at least 3 months after stopping COTELLIC.
 - Talk to your healthcare professional about birth control methods that may be right for you.
 - Tell your healthcare professional right away if you become pregnant or think you are pregnant during treatment with COTELLIC.
- are breastfeeding or plan to breastfeed. It is not known if COTELLIC passes into your breast milk. You and your healthcare professional should decide if you will take COTELLIC or breastfeed. You should not do both.

Other warnings you should know about during treatment:

- **Driving and using machines:** COTELLIC can affect your ability to drive or use machines. Avoid driving, using tools or operating machines if you have problems with your vision or other problems that might affect your ability, e.g. if you feel dizzy or tired. Talk to your doctor if you are not sure.
 - **Increased Sensitivity to Sunlight:** Avoid sunlight while you are taking COTELLIC. COTELLIC in combination with ZELBORAF can make your skin sensitive to sunlight. You may burn more easily and get severe sunburns. To help protect against sunburn:
 - When you go outside, wear clothes that protect your skin, including your head, face, hands, arms, and legs.
 - Use lip balm and a broad-spectrum sunscreen with SPF 30 or higher.
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- **Lactose:** COTELLIC contains lactose (a type of sugar). If you have been told by your healthcare professional that you have intolerance to lactose, talk to your healthcare professional before taking this medicine.
- **Children and adolescents:** COTELLIC is not recommended for children and adolescents. The effects of COTELLIC in people younger than 18 years old are not known.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with COTELLIC:

Some types of medicines can affect a type of protein in the body called CYP3A. This protein breaks down COTELLIC in the body. Use of these medicines while on COTELLIC may make it more likely that you will have side effects, or may affect how COTELLIC works.

- Drugs used to treat fungal infections (itraconazole, ketoconazole, posaconazole, voriconazole, fluconazole, miconazole)
- Antibiotics used to treat infections (clarithromycin, erythromycin, rifampin)
- Drugs used to treat HIV infection (lopinavir, ritonavir, fosamprenavir, delavirdine, efavirenz, etravirine)
- Drugs used to treat heart problems (amiodarone, diltiazem, verapamil)
- Drugs used to treat seizures (fits) (carbamazepine, phenytoin)
- Bosentan, used to treat high blood pressure in the blood vessels between the heart and the lungs
- Modafinil, used to treat sleep disorders
- Imatinib, an anti-cancer drug
- Cyclosporine, used to decrease your body's immune reaction
- St. John's Wort (*Hypericum perforatum*) used to treat depression and other conditions
- You should not drink grapefruit juice, eat grapefruit or take any products containing grapefruit extract while you are on COTELLIC in combination with ZELBORAF.

How to take COTELLIC:

- Always take COTELLIC exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Swallow COTELLIC tablets whole with a glass of water.
- COTELLIC can be taken with or without food.

Usual adult dose:

- The recommended dose of COTELLIC is 60 mg (3 tablets) taken once daily for 21 days, followed by a 7 day break with no COTELLIC treatment (28 day cycle – 3 weeks on, 1 week off).
- During the 7 day break with no COTELLIC treatment, you should keep taking ZELBORAF as directed by your healthcare professional.
- Start your next COTELLIC treatment cycle after the 7 day break.

Vomiting:

If you vomit (throw up) after taking COTELLIC, do not take an extra dose of COTELLIC on that day. Continue to take COTELLIC as normal, the next day.

Overdose:

If you think you have taken too much COTELLIC, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take COTELLIC and:

- If it is more than 12 hours before your next dose, take the missed dose as soon as you remember.
- If it is less than 12 hours before your next dose, skip the missed dose. Take the next dose at the usual time.
- Do not take a double dose to make up for a missed dose.

What are possible side effects from using COTELLIC?

These are not all the possible side effects you may feel when taking COTELLIC. Tell your healthcare professional if any of the side effects listed bothers you or does not go away. If you experience any side effects not listed here, contact your healthcare professional. Please also see the warnings above.

Very common side effects of COTELLIC – these may affect more than 1 in 10 people:

- Vomiting
- Nausea
- Abdominal pain
- Fever
- Chills
- Swelling of the arms or legs
- Skin rash with a flat discoloured area or raised bumps that looks like acne
- Muscle aches

See also the table below called *Serious side effects and what to do about them*.

Common side effects of COTELLIC – these may affect up to 1 in 10 people:

- Increased sugar level (shown in blood tests)
- Dehydration
- Dizziness
- Mouth sores, including those caused by the herpes virus (cold sores)
- Dry mouth
- Hives
- Common cold (sore throat, stuffy and / or runny nose)
- Yeast infections
- Swelling, pain and redness of the palm of hand and sole of foot
- Small red bumps or pimples around hair follicles which may be itchy or tender
- Tender and red bumps under the skin due to inflammation of the layer of fat under the skin
- Swelling, redness and itching of the eye
- Muscle weakness

See also the table below called *Serious side effects and what to do about them*.

Your healthcare professional will take blood tests while you are taking COTELLIC. The most common changes to blood tests include:

- increased blood levels of liver enzymes (GGT, ALT, or AST)
 - decreased blood levels of albumin (a protein made by the liver)
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- increased blood level of bilirubin (a yellow pigment in the blood)
- increased blood level of an enzyme from the pancreas called lipase
- increased blood level of an enzyme called lactate dehydrogenase
- increased blood level of enzyme from muscle [creatinine phosphokinase (CPK)]
- decreased blood level of phosphate, sodium or potassium
- increased blood level of sodium
- increased blood level of cholesterol
- increased blood level of liver or bone enzyme (alkaline phosphatase)
- decreased blood level of a type of white blood cell (lymphocyte)
- decreased blood level of red blood cells (anemia)

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	Stop taking drug and get immediate medical help
VERY COMMON Diarrhea: increased number of stools, loose or watery stools	✓	
Hypertension (high blood pressure): new or worsening high blood pressure, severe headache, lightheadedness, dizziness	✓	
Photosensitivity (increased sensitivity to sunlight): red, painful, itchy skin that is hot to touch (sunburn), sun rash, skin irritation, bumps or tiny papules, thickened, dry, wrinkled skin	✓	
COMMON Eye problems: blurred vision, distorted vision, partly missing vision, halos, any other vision changes. These problems can arise from: <ul style="list-style-type: none"> • Serous retinopathy (a build-up of fluid under the retina of the eye) • Separation of the retina (the area of the eye responsible for sight) from its connection at the back of the eye • Retinal vein occlusion (a blockage in a blood vessel carrying blood away from the retina): blurred or reduced vision, usually affects one eye, can occur suddenly 	✓	
Heart problems: These problems can arise from: <ul style="list-style-type: none"> • Left ventricular dysfunction (inadequate pumping of blood by the heart): persistent coughing or wheezing, shortness of breath, tiredness, increased heart rate, swelling of your ankles and feet • Atrial fibrillation (irregular heartbeat): feeling that your heart is racing or fluttering, weakness, decreased ability to exercise, tiredness, dizziness, lightheadedness, confusion, difficulty breathing, chest pain 	✓	
Bleeding problems: blood in the urine, unusual or excessive vaginal bleeding, bleeding of the gums, abdominal pain, red or black stools that look like tar, headache, dizziness, or feeling weak.	✓	

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	Stop taking drug and get immediate medical help
Allergic reactions: itchy rash, hives, redness of skin, swelling of the face, lips, tongue, or throat, difficulty swallowing or breathing		✓
Rash: a rash that covers a large area of your body, blisters, or peeling skin	✓	
Pneumonitis (inflammation of the lungs): difficulty breathing, may be accompanied by cough, fever or chills	✓	
Basal-cell carcinoma, cutaneous squamous cell carcinoma, and keratoacanthoma (types of skin cancer): new wart, skin sore or reddish bump that bleeds or does not heal	✓	
Abnormal liver test or liver injury: yellowing of your skin or the white of your eyes, dark or brown (tea coloured) urine, nausea or vomiting, feeling tired or weak, loss of appetite	✓	
Increased serum creatine phosphokinase (CPK) levels (increased blood levels of an enzyme from muscle) and rhabdomyolysis (a rapid breakdown of muscle): unexplained muscle aches, muscle spasms and weakness, dark, reddish-coloured urine.	✓	
UNCOMMON New primary melanoma: mole which has irregular shape, border, or colour, is growing, or changing shape or colour	✓	

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect™ (<http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php>);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 1908C
Ottawa, ON
K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect™ (<http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php>).

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Keep out of reach and sight of children.
- Store COTELLIC between 15-30°C.

- Do not take this medicine after the expiry date which is stated on the blister pack after “EXP”. The expiry date refers to the last day of that month.
- Do not throw away any unused medicine in the garbage or down the drain or toilet. Ask your pharmacist how to best dispose of medicines that you no longer require. These measures will help to protect the environment.

If you want more information about COTELLIC:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website \(http://hc-sc.gc.ca/index-eng.php\)](http://hc-sc.gc.ca/index-eng.php); the manufacturer’s website (www.rochecanada.com), or by calling 1-888-762-4388.

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Hoffmann-La Roche Limited
Mississauga, ON L5N 5M8