

PART III: CONSUMER INFORMATION

Pr**REVOLADE**[®] eltrombopag tablets (as eltrombopag olamine)

This leaflet is part III of a three-part "Product Monograph" published when REVOLADE was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about REVOLADE. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Chronic immune thrombocytopenia (ITP): REVOLADE is used to treat a bleeding disorder known as chronic immune thrombocytopenia (ITP) to increase platelet counts in adults and children one year of age and older when other medications have not worked. ITP is a condition where there is a low platelet count (thrombocytopenia). Platelets are blood cells that help the blood clot normally. ITP patients may have an increased risk of bleeding. Symptoms of bleeding are petechiae (pinpoint sized flat round red spots under the skin), purpura (bruising), nosebleeds, bleeding gums, or not being able to control bleeding if cuts or injuries occur.

Severe Aplastic Anemia (SAA):

REVOLADE is used to treat adult patients with low blood counts caused by severe aplastic anemia (SAA). REVOLADE is used when other drugs don't work.

Chronic hepatitis C (HCV) Associated Thrombocytopenia: Many patients with HCV infections have low platelet counts (thrombocytopenia) not only as a result of the disease but also due to some of the medicines that are used to treat the disease. The use of REVOLADE to increase and maintain the platelet count prior to and throughout antiviral treatment of HCV infection gives patients a better opportunity to maintain the optimal dose and duration of their antiviral therapy.

What it does:

Treatment of ITP:

REVOLADE is a drug that may help increase the number of platelets.

Treatment of SAA:

REVOLADE is a drug that may help increase the number of platelets and other types of blood cells.

Treatment of HCV Associated Thrombocytopenia:

REVOLADE is a drug that may help increase the number of platelets.

When it should not be used:

Do not use REVOLADE if you:

- are allergic to REVOLADE or to any of the non-medicinal ingredients
- have severe liver impairment

What the medicinal ingredient is:

eltrombopag

What the nonmedicinal ingredients are:

Tablets: Hypromellose, macrogol, magnesium stearate, mannitol, microcrystalline cellulose, povidone, sodium starch glycolate and titanium dioxide.

12.5 mg and 25 mg tablets also contain polysorbate.

50 mg tablets also contain iron oxide yellow and iron oxide red.

75 mg tablets also contain iron oxide red and iron oxide black.

What dosage forms it comes in:

Tablets: 12.5 mg, 25 mg, 50 mg, and 75 mg.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Chronic hepatitis patients with liver disease may be at increased risk of liver failure and death when taking REVOLADE with pegylated interferon and ribavirin, which are used to treat hepatitis C. Your doctor may monitor your liver symptoms closely.

REVOLADE is only available as tablets and should not be used in patients who are unable to swallow REVOLADE tablets whole.

Consult the Consumer Information for both pegylated interferon and ribavirin for relevant safety information associated with the use of these products as they are used with REVOLADE when treating patients with hepatitis C and thrombocytopenia.

BEFORE you use REVOLADE, talk to your doctor or pharmacist if you:

- Have liver problems.
- Have kidney problems.
- Have a history of thrombosis (formation of a clot inside a blood vessel, obstructing the flow of blood), or you know that thrombosis occurs frequently in your family. The risk of blood clots may be increased in the following circumstances: If you are elderly, if you have been bedridden for a long time, if you have cancer, if you are taking the contraceptive birth control pill, or hormone replacement therapy, if you have undergone recent surgery or received a physical injury, if you are overweight, if you are a smoker.
- Have a history of cataracts (problems with sight).
- Are pregnant or plan to become pregnant.
- Are breast-feeding or planning to breastfeed.
- Are over 65 years of age.
- Are of East Asian descent.

Pregnancy:

You should avoid becoming pregnant while taking REVOLADE because the effect of REVOLADE on pregnancy is not known. You should use a reliable method of contraception (a way to prevent you from becoming pregnant). If you become pregnant during treatment, tell your doctor.

Breast-feeding:

Studies in animals have shown that REVOLADE is likely secreted into milk. It is not known whether REVOLADE passes into breast milk. Breast-feeding is not recommended while you are taking REVOLADE.

Cataracts:

In animal studies it was found that REVOLADE caused the development of cataracts (a clouding of the lens in the eye). In HCV studies in patients with thrombocytopenia (low blood platelet count) also receiving interferon, an increased risk in the incidence of cataracts has also been seen. In chronic ITP studies, new cataracts have happened in patients receiving REVOLADE. In the chronic ITP studies with children, two cataract events occurred in patients given REVOLADE. Your doctor may recommend that you are checked for cataracts before and during REVOLADE therapy.

INTERACTIONS WITH THIS MEDICATION

Taking Other Medicines:

There are certain groups of medicines, including prescription and non-prescription medicines and vitamins that interact with REVOLADE and that you should not take

at the same time while receiving a course of REVOLADE. These medications include some products within the following groups:

- Antacid medicines to treat stomach ulcers, indigestion or heartburn
- Certain medicines used to lower cholesterol (statins)
- Minerals such as aluminum, calcium, iron, magnesium, selenium and zinc which may be found in mineral supplements

There are certain groups of medicines, requiring additional platelet monitoring. These medicines include lopinavir/ritonavir (medicines to treat HIV infection) and cyclosporine (used in the context of transplantations or immune diseases).

Talk to your doctor if you take any of these medications. In some cases, you may need to adjust the dose or alter the timing of the dose (see Usual dose). Ask your doctor or pharmacist to review the medicines you are currently taking and suggest suitable alternatives if necessary.

If you are also taking medicines which are given to prevent blood clots (anticoagulants or antiplatelet therapy), there is a greater risk of bleeding. You should discuss this with your doctor. If you are taking other medications for your treatment, these may be reduced or stopped when given together with REVOLADE.

Taking REVOLADE with Food and Drink:

Do not take REVOLADE with dairy products (e.g. milk, ice cream, yogurt, etc.).

REVOLADE may be taken with food low in calcium such as:

- Fruits such as pineapple, raisins and strawberries
- Lean ham, chicken or beef
- Unfortified fruit juice, soy milk and grain. (Unfortified means no added calcium, magnesium or iron).

Please discuss this matter with your doctor or pharmacist; they will be able to give you advice on the most suitable meals to be eaten while you are taking REVOLADE.

PROPER USE OF THIS MEDICATION

Swallow the tablets whole, with some water. Do NOT crush tablets and then mix with food or liquids.

Usual adult dose (18 years and above):

The usual starting dose for either adult ITP or adult SAA patients is **50 mg** REVOLADE once daily. People of East Asian / Southeast Asian origin (Chinese, Japanese, Taiwanese, Thai, or Korean) need to start at a lower dose of 25 mg.

The usual starting dose for adult HCV patients is **25 mg** REVOLADE once daily. People of East Asian / Southeast Asian origin (Chinese, Japanese, Taiwanese, Thai or Korean) will start on the same 25 mg dose.

Usual dose for pediatric ITP patients (aged 1 to less than 18 years):

The usual starting dose for pediatric ITP patients 1 to 5 years of age is **25 mg** REVOLADE once daily.

The usual starting dose for pediatric ITP patients 6 to less than 18 years of age is **50 mg** REVOLADE once daily. Pediatric ITP patients 6 to less than 18 years of age of East Asian / Southeast Asian origin (Chinese, Japanese, Taiwanese, Thai, or Korean) need to start at a lower dose of 25 mg.

If your child is not able to swallow the tablets whole, talk to your doctor or your pharmacist.

If you have liver disease and your doctor has decided to treat you for either ITP or SAA, your starting dose should be no more than 25 mg taken once daily.

Based on your response to REVOLADE your doctor will adapt the dose and may recommend that your daily dose of REVOLADE be increased or decreased.

ITP Patients: The dose of REVOLADE should not exceed 75 mg/day.

SAA Patients: The dose of REVOLADE should not exceed 150 mg/day.

HCV Associated Thrombocytopenia Patients: The dose of REVOLADE should not exceed 100 mg/day.

Do not stop taking REVOLADE until your doctor advises you to do so.

After your doctor advises you to stop treatment with REVOLADE, your platelet count will then be checked each week for 4 weeks.

Don't take REVOLADE during the 2 hours before or 4 hours after you take antacid medication (to treat indigestion), mineral supplements (such as aluminium, calcium, iron, magnesium, selenium or zinc), or dairy products. If you do, the medicine will not be properly absorbed into your body. One way to avoid issues with

these products would be to take them in the morning and take REVOLADE in the evening. Ask your doctor or pharmacist for advice if you are unsure.

Adult ITP Patients: Do not take REVOLADE for more than one year at a time. Treatment should be reassessed by your doctor after one year.

HCV Associated Thrombocytopenia Patients: Do not take REVOLADE for more than one year at a time. Once your anti-viral therapy has been discontinued treatment with REVOLADE will be stopped.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose, take it as soon as you remember. However, do not take a double dose to make up for a forgotten dose, instead start taking REVOLADE again at the regular time the next day.

If you have any further questions on the use of REVOLADE, ask your doctor or pharmacist.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, REVOLADE can cause side effects, although not everybody gets them.

Side effects reported with REVOLADE in the treatment of adult patients with ITP include:

Common side effects

- Nausea
- Diarrhea
- Dry mouth
- Vomiting
- Rash
- Joint pain
- Dry eye
- Feeling hot
- Headache
- Numbness or tingling of the skin
- Increased sweating
- Sore throat or discomfort when swallowing
- Cataract
- Fatigue

Common side effects that may show up in the blood tests

- Changes in enzymes produced by the liver
- Increase in bilirubin (a substance produced by the liver)

Side effects reported with REVOLADE in the treatment of children 1 year and older with ITP include:

Very common side effects

- Sore throat, runny nose, nasal congestion and sneezing
- Infection in the nose, sinuses, throat and upper airways, common cold (*upper respiratory tract infection*)
- Cough

Common side effects

- Abdominal pain, diarrhoea, constipation, nausea, indigestion
- Toothache, bleeding from the mouth
- Decreased appetite
- Pain in the mouth and throat
- Fever
- Lung or skin infection, influenza, meningitis, enlarged tonsils, head lice
- Rash, itchy rash, scratching, bruising
- Vitamin D deficiency
- Anaemia
- Motion sickness
- Changes in the back of the eye (retina)
- Pain, back pain, groin pain, osteoporosis, non-cardiac chest pain, skin or joint injury
- Lack of energy, sleepiness
- Numbness
- Eating disorder
- Allergic reaction

Common side effects that may show up in the blood tests

- Changes in enzymes produced by the liver

Side effects reported with REVOLADE in the treatment of patients with SAA include:

Very common side effects

- Cough, shortness of breath, runny nose, pain in the nose and throat
- Anxiety and Depression
- Fever
- Headache, dizziness, fatigue (feeling very tired)
- Abdominal pain, diarrhea, nausea
- Bruising

- Muscle spasms, joint pain
- Pain in arms, legs, hands and feet

Very common side effects that may show up in the blood tests

- Increase in some liver enzymes (transaminases)

Common side effects

- Bleeding from the gums
- Pain or blisters inside the mouth
- Vomiting
- Weakness, lack of energy
- Chills
- Swelling of arms and legs
- Shortness of breath when walking
- Nosebleed
- Back pain
- Skin rash, itching, rash with pale red, raised, itchy bumps
- Patch of skin that looks different
- Dry eyes
- Trouble sleeping
- Feeling unwell, feeling pain
- Constipation, passing gas
- Abnormal colour of urine or feces
- Pain when swallowing
- Swollen tongue
- Decreased or increased appetite
- Pain in bones
- Muscle pain
- Cataract

Common side effects that may show up in the blood tests

- High levels of iron in your blood
- Low blood sugar levels
- Changes in enzymes produced by the liver

Laboratory tests may show abnormal changes to the cells in your bone marrow.

Side effects reported with REVOLADE in the treatment of patients with HCV include:

Common side effects

- Fever
- Fatigue
- Chills
- Headache
- Cough
- Nausea
- Diarrhea

- Unusual hair loss or thinning
- Muscle pain
- Itching
- Feeling weak
- Difficulty sleeping
- Loss of appetite
- Flu-like symptoms
- Swelling of the hands, ankles or feet
- Cataract

Very common side effects that may show up in the blood tests

- Reduced number of red blood cells (*anemia*)

Common side effects that may show up in the blood tests

- Increase in bilirubin (a substance produced by the liver)

Frequency not known: (frequency cannot be estimated from the available data from spontaneous reports)

- Yellowing or darkening of skin (skin discolouration)

Please talk with your doctor if you experience skin discolouration as they can evaluate and manage this side effect appropriately.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate medical help
		Only if severe	In all cases	
Very common	Febrile neutropenia: fever, flu-like symptoms, shaking chills, severe night sweats		✓	
Common	Sepsis: rapid heartbeat, fever, shaking chills, rapid breathing, nausea, vomiting, decreased urination		✓	
	Viral infection: fever, fatigue, headache, body aches, diarrhea, nausea, vomiting		✓	
	Eye disorders: -Cataracts: clouded, blurred or dim vision, seeing halos around lights, fading or yellowing of colours -Blurred Vision -Visual impairment: changes in vision -Vitreous floaters: spots in vision that appear as specks or strings of floating material; spots that move with eye movement		✓	
	Abdominal discomfort		✓	
	Splenic infarction (spleen tissue death): severe pain in upper left side of abdomen that can radiate to left shoulder		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate medical help
	Only if severe	In all cases	
Syncope and dizziness postural: fainting, dizziness when standing up or sitting down		✓	
Liver Problems (including Hepatitis B): yellow colour to skin, whites of the eyes (jaundice), unusual dark urine, unusual tiredness, right upper stomach area pain		✓	
Hypoglycemia (low blood sugar): thirst, frequent urination, hunger, nausea and dizziness, fast heartbeat, tingling trembling, nervousness, sweating		✓	
Uncommon Allergic reactions: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing		✓	
Bleeding		✓	
Blood clot in the leg: swelling, pain or tenderness of one leg		✓	
Unusual hair loss or thinning		✓	
Musculoskeletal chest pain		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate medical help
	Only if severe	In all cases	
Musculoskeletal pain (pain that affects the muscles and tendons along with bones)		✓	
Myalgia (aching muscles)		✓	
Urinary tract infections		✓	

REVOLADE may cause serious side effects

Liver Problems:

REVOLADE may damage your liver and cause serious, even life threatening, illness. You must have blood tests to check your liver before you start taking REVOLADE and during treatment. When you are given antiviral treatments together with REVOLADE to treat HCV associated thrombocytopenia, some liver problems can get worse.

Your doctor will order the blood tests and any other tests required. In some cases, REVOLADE treatment may need to be stopped.

Bleeding after you stop treatment:

When you stop taking REVOLADE, your blood platelet count may drop back down to what it was before you started taking REVOLADE. These effects are most likely to happen within 4 weeks after you stop taking REVOLADE. The lower platelet counts may increase your risk of bleeding. Your doctor will check your platelet counts for at least 4 weeks after you stop taking REVOLADE. Tell your doctor or pharmacist if you have any bruising or bleeding after you stop taking REVOLADE.

Problems with your bone marrow:

People with the disease for which you are being treated may have problems with their bone marrow. Drugs like REVOLADE help increase the number of platelets. This can increase the risk of bone marrow cell disorders, blood cancers, changes in DNA, or cause scarring of the bone marrow. Signs of bone marrow changes may show up as abnormal results in your blood tests. Your doctor may also carry out tests to directly check your bone marrow during treatment with REVOLADE.

High platelet counts and higher chance for blood clots:

You have a higher chance of getting a blood clot if your platelet count is too high during treatment with REVOLADE, but blood clots can occur with normal or even low platelet counts. If you have disease of the liver, you are at risk of a blood clot in a blood vessel that feeds your liver (portal vein thrombosis). You may have severe complications from some forms of blood clots, such as clots that travel to the lungs or that cause heart attacks or strokes. You may have clots in small blood vessels, which may harm organs such as the kidneys. Your doctor will check your blood platelet counts, and change your dose or stop REVOLADE if your platelet counts get too high. Tell your doctor right away if you have any of these signs and symptoms of a blood clot: swelling or pain/tenderness of one leg, sudden shortness of breath especially when accompanied with sharp pain in the chest and/or rapid breathing, abdominal pain, enlarged abdomen, blood in stool.

This is not a complete list of side effects. For any unexpected effects while taking REVOLADE contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of reach of children.

Tablets: Store below 30°C, protect from freezing.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at**
www.healthcanada.gc.ca/medeffect
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
 - **Fax toll-free to 1-866-678-6789, or**
 - **Mail to:**
Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.novartis.ca> or by contacting the sponsor,

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