NOVARTIS

Revolade 25 mg and 50 mg

Eltrombopag

Patient Information Leaflet

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REVOLADE® 25 mg and 50 mg Film-coated Tablet

(eltrombopag)

Read all of this leaflet carefully before you start taking REVOLADE

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- REVOLADE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1 What REVOLADE is and what it is used for

REVOLADE contains eltrombopag, which belongs to a group of medicines called thrombopoietin receptor agonists. It is used to help increase the number of platelets in your blood.

What REVOLADE is used for

REVOLADE is a medicine that may help to increase the number of platelets, a type of blood cell that helps to reduce or prevent bleeding.

It is used to treat a bleeding disorder known as immune (primary) thrombocytopenia (ITP) in patients aged 1 year and above who have already taken other medicines (corticosteroids or immunoglobulins), which have not worked.

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REVOLADE may also be used to treat adult patients with low blood counts caused by severe aplastic anaemia (SAA). SAA is a disease in which the bone marrow is damaged, causing a deficiency of the red blood cells (anaemia), white blood cells (leukopenia) and platelets (thrombocytopenia).

2 What you need to know before you take REVOLADE

Do not take REVOLADE if you:

- are allergic (hypersensitive) to eltrombopag olamine, or any of the excipients of REVOLADE
- are pregnant or plan to become pregnant
- are breastfeeding.

Warnings and precautions

Talk to your doctor before taking REVOLADE:

- if you have liver problems. People who have low platelet counts as well as advanced chronic (long-term) liver disease are more at risk of side effects, including life-threatening liver damage and blood clots. If your doctor considers that the benefits of taking REVOLADE outweigh the risks, you will be closely monitored during treatment
- If you have a history of thrombosis (formation of a clot inside a blood vessel, obstructing the flow of blood), or you know that thrombosis has occurred in your family:

  You may be at higher risk of blood clots:
  - as you get older
  - if you have had to stay in bed for a long time
  - if you have cancer
  - if you are taking the contraceptive birth control pill or hormone replacement therapy
  - if you have recently had surgery or sustained a physical injury
  - if you are very overweight (obese)
  - if you are a smoker
  - if you have advanced chronic liver disease

  If any of these apply to you, **tell your doctor** before starting treatment. You should not take REVOLADE unless your doctor considers that the expected benefits outweigh the risk of blood clots.
- If you have cataracts (the lens of the eye getting cloudy)
- have problems with your bone marrow
- have bleeding after you stop treatment
- have kidney disease.

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. Your doctor will order these blood tests. In some cases REVOLADE treatment may need to be stopped.

Bleeding after you stop treatment:

When you stop taking REVOLADE, your blood platelet count will 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.

Problems with your bone marrow:

People with the disease for which you are being treated may have problems with their bone marrow. REVOLADE could make this problem worse. 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. 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. Your doctor will check your blood platelet counts, and change your dose or stop REVOLADE if your platelet counts get too high.

Get medical help immediately if you have any of these signs of a blood clot:

- swelling, pain or tenderness in one leg
- sudden shortness of breath especially together with sharp pain in the chest or rapid breathing
- abdominal (stomach) pain, enlarged abdomen, blood in your stools

Cataracts:

Your doctor may recommend that you are regularly checked for cataracts (at least every six months).

Older people (65 years and above:)

There are limited data on the use of REVOLADE in patients aged 65 years and older. Care should be taken when using REVOLADE if you are aged 65 years or above.

Children and adolescents:

REVOLADE is not recommended for children aged under 1 year who have ITP. It is also not recommended for people under 18 years with low platelet counts due to hepatitis C or severe aplastic anaemia.

Other medicines and REVOLADE

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.).

There are certain groups of medicines, including prescription and non-prescription medicines as well as vitamins and minerals that interact with REVOLADE that you should not take at the same time or that require a dose adjustment while receiving a course of REVOLADE. These medications include some products within the following groups:

- antacid medicines to treat stomach ulcers or heartburn
- certain medicines used to lower cholesterol (statins)
- minerals such as aluminium, 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 cyclosporin (used in the context of transplantations or immune diseases).

Your doctor will review the medicines you are currently taking to make sure you are not taking something that cannot be taken with the REVOLADE. If you require any of these medications and a suitable substitute is not available, please discuss this with your doctor.

Taking REVOLADE with food and drink:

REVOLADE absorption is affected by calcium intake. 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; they will be able to advise on the most suitable meals to be eaten while you are taking REVOLADE.

Don’t take REVOLADE during the 2 hours before or 4 hours after you take antacid medication to treat indigestion or, mineral supplements, such as aluminium, calcium, iron, magnesium, selenium or zinc, dairy products such as cheese, butter, yoghurt or ice-cream. 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 REVOLADE in the evening. Ask your doctor or pharmacist for advice if you are unsure.

Pregnancy and Breastfeeding

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking REVOLADE.

- You should not take REVOLADE if you are pregnant as it is contra-indicated.
- You should avoid becoming pregnant while taking REVOLADE.
- If you become pregnant during treatment, tell your doctor.
- You should not breastfeed while you are taking REVOLADE.

Driving and using machines

REVOLADE can make you dizzy and have other side effects that make you less alert. Don’t drive or use machines unless you are sure you’re not affected.

3 How to take REVOLADE

Always take REVOLADE exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

REVOLADE should be taken at least 2 [4] hours before or at least 4 hours after taking antacids, dairy products or some other mineral supplements such as aluminium, calcium, iron, magnesium, selenium and zinc. One way to avoid issues with these products would be to take them in the morning and REVOLADE in the evening.

How much to take

For ITP

Adults and children (6 to 17 years) – the usual starting dose for ITP is one 50 mg REVOLADE tablet a day. If you are of East/Southeast-Asian origin you need to start at a lower dose of 25 mg.

Children (1 to 5 years) — the usual starting dose for ITP is one 25 mg tablet of REVOLADE a day.

For SAA

Adults - the usual starting dose for SAA is one 50 mg tablet of REVOLADE a day. If you are of East/Southeast-Asian origin you need to start at a lower dose of 25 mg.

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.

Please expect that at the beginning of therapy your platelet count and other routine blood parameters will need to be monitored frequently. Your doctor will also carry out blood tests to check your liver function before and during treatment with REVOLADE.

How to take Revolade tablets

Swallow the tablet whole, with some water.

When to take Revolade

Make sure that –

- in the 4 hours before you take Revolade
- and the 2 hours after you take Revolade

You don’t consume any of the following:

- dairy foods such as cheese, butter, yoghurt or ice cream
- milk or milk shakes, drinks containing milk, yoghurt or cream
- antacids, a type of medicine for indigestion and heartburn
- some mineral and vitamin supplements including iron, calcium, magnesium, aluminium, selenium and zinc

If you do, the medicine will not be properly absorbed into your body.

If you take more REVOLADE than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If possible show them the pack, or this leaflet. You will be monitored for any signs or symptoms of side-effects and given appropriate treatment immediately.

If you forget to take REVOLADE:

Do not take a double dose to make up for a forgotten dose on a given day; simply resume your dosing with the next scheduled dose the following day.

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

Once you have started using REVOLADE:

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

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

If you have any problems/questions regarding the use of REVOLADE, please consult with your doctor.

4 Possible Side-effects

REVOLADE can cause side-effects.

Not all side-effects reported for REVOLADE are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop taking REVOLADE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side-effects. If you have them, you may have had a serious allergic reaction to REVOLADE. You may need urgent medical attention or hospitalisation.

REVOLADE may cause serious side-effects: Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Liver problems: REVOLADE may damage your liver and cause serious, even life-threatening, illness. Tell your doctor right away if you have any of these signs and symptoms of liver problems:

- yellowing of the skin or the whites of the eyes (jaundice)
- unusual darkening of the urine
- unusual tiredness
- right upper stomach area pain.

- Bleeding after you stop treatment: When you stop taking REVOLADE, your blood platelet count will drop back down to what it was before you started taking REVOLADE. Tell your doctor or pharmacist if you have any bruising or bleeding after you stop taking 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. Tell your doctor right away if you have signs and symptoms of a blood clot in the leg, such as swelling or pain/tenderness of one leg.

These are all serious side-effects. You may need urgent medical attention.

The following side-effects have been reported to be associated with treatment with REVOLADE in adult patients with ITP.

Frequent side effects

- common cold
- feeling sick (nausea)
- diarrhoea
- cough
- infection in the nose, sinuses, throat and upper airways, common cold (upper respiratory tract infection)
- muscle pain, muscle spasm, muscle weakness
- back pain
- bone pain
- heavy menstrual period
- sore throat and discomfort when swallowing
- eye problems including abnormal eye test, dry eye, eye pain and blurred vision
- vomiting
- flu (influenza)
- cold sore
- pneumonia
- irritation and inflammation (swelling) of the sinuses
- inflammation (swelling) and infection of the tonsils infection of the lungs, sinuses, tonsils, nose and throat, bladder
- inflammation of the gum tissue

- loss of appetite
- feeling of tingling, prickling or numbness, commonly called “pins and needles”
- feeling drowsy
- ear pain
- pain, swelling and tenderness in one of your legs (usually the calf) with warm skin in the affected area (signs of a blood clot in a deep vein)
- localised swelling filled with blood from a break in a blood vessel (haematoma)
- mouth problems including dry mouth, sore mouth, sensitive tongue, bleeding gums, mouth ulcers
- runny nose
- toothache
- stomach pain and tenderness
- liver problems
- skin changes including excessive sweating, itching bumpy rash, red spots, changes in appearance of the skin
- hair loss
- foamy, frothy or bubbly-looking urine (signs of protein in urine)
- generally feeling unwell, have a high temperature, feeling hot
- chest pain
- problems sleeping, depression
- migraine
- decreased vision
- spinning sensation (vertigo)
- digestive wind/gas

The following additional side effects have been reported to be associated with treatment with REVOLADE in children (aged 1 to 17 years) with ITP:

If these side effects become severe, please tell your doctor, pharmacist or nurse.

Frequent side effects

- infection in the nose, sinuses, throat and upper airways, common cold (upper respiratory tract infection)
- diarrhoea
- abdominal pain
- cough
- high temperature
- feeling sick (nausea)
- difficulty in sleeping (insomnia)
- toothache

- pain in the nose and throat
- itchy, runny or blocked nose
- sore throat, runny nose, nasal congestion and sneezing
- mouth problems including dry mouth, sore mouth, sensitive tongue, bleeding gums, mouth ulcers

The following side effects have been reported to be associated with treatment with REVOLADE in patients with severe aplastic anaemia (SAA):

If these side effects become severe, please tell your doctor, pharmacist or nurse.

Frequent side effects

- cough
- headache
- pain in the nose and throat
- diarrhoea
- nausea
- joint pain (arthralgia)
- pain in extremities (arms, legs, hands and feet)
- dizziness
- feeling very tired (fatigue)
- fever
- chills
- itchy eyes
- blisters in the mouth
- abdominal pain
- muscle spasms
- anxiety
- depression
- feeling cold
- feeling unwell
- eye problems including blurred vision, cloudy lens in the eye (cataract), spots or deposits in eye (vitreous floaters), dry eye, itchy eye, yellowing of the whites of the eyes or skin
- nose bleeds
- bleeding of the gums
- digestive system problems including being sick (vomiting), change in appetite (increased or decreased), stomach pain/discomfort, swollen stomach, passing wind, change in stool colour
- fainting

- skin problems including small red or purple spots caused by bleeding into the skin (petechiae) rash, itching, skin lesion
- back pain
- muscle pain
- bone pain
- weakness (asthenia)
- swelling of the lower limbs due to the accumulation of fluids
- abnormal coloured urine
- interruption in blood supply to spleen (splenic infarction)
- runny nose

Reporting of side effects

If you any get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications /Index/8. By reporting side effects, you can help provide more information on the safety of REVOLADE.

5 How to store REVOLADE

Store all medicines out of reach of children.

Store at or below 30 °C.

Do not remove blisters from the carton until required for use.

Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6 Contents of the pack and other information

What REVOLADE contains

Each film-coated tablet contains the active substance eltrombopag olamine equivalent to either 25 mg or 50 mg of eltrombopag as eltrombopag free acid.

The other ingredients include:

Tablet Core: Magnesium stearate, mannitol, microcrystalline cellulose, povidone and sodium starch glycolate.

Contains sugar (mannitol): 29,7 mg per REVOLADE 25 mg tablet and 59,5 mg per REVOLADE 50 mg tablet.

Tablet Coating: Hypromellose, macrogol 400, titanium dioxide, polysorbate 80 (25 mg tablets only), iron oxide yellow (50 mg tablet only) and iron oxide red (50 mg tablet only).

What REVOLADE looks like and contents of the pack

What REVOLADE looks like:

25 mg: white, round, biconvex film-coated tablet with identity code 'GS NX3' and '25' debossed on one side.

50 mg: brown, round, biconvex film coated tablet with identity code 'GS UFU' and '50' debossed on one side.

Contents of the pack

REVOLADE tablets are packed into silver aluminium-foil blister strips containing 7 tablets each.

The blister strip comprises an orientated polyamide / aluminium foil / polyvinyl chloride (PVC) laminate sealed with an aluminium foil lidding with a vinyl acrylic seal coating.

Two or four blister strips are packed into a carton giving a 14 or 28 tablet pack respectively.

Holder of Certificate of Registration

Novartis South Africa (Pty) Ltd

Magwa Crescent West

Waterfall City, Jukskei View

Johannesburg, 2090

South Africa

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Note: The Professional Information has been made available to your healthcare provider.