

Promacta in Pediatric Patients 1 Year of Age and Older With Chronic Immune Thrombocytopenia (ITP)

ABOUT PROMACTA

In August 2015, the US Food and Drug Administration (FDA) approved an expanded use for Promacta[®] (eltrombopag), the once-daily oral thrombopoietin (TPO) receptor agonist, to include children 1 year of age and older with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. The updated label also includes a new oral suspension formulation of Promacta that is designed for younger children who may not be able to swallow tablets. Promacta is also FDA-approved for¹:

- thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
- thrombocytopenia in patients with chronic hepatitis C virus (HCV) infection to allow the initiation and maintenance of interferon-based therapy
- severe aplastic anemia in patients who have had an insufficient response to immunosuppressive therapy

Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding, and in people with chronic hepatitis C whose low blood platelet counts keep them from starting or continuing interferon-based therapy. It is not known if Promacta is safe and effective when used with other antiviral medicines that are approved to treat chronic hepatitis C.

Eltrombopag is marketed under the brand name Promacta[®] in the US and Revolade[®] in most countries outside the US. In the EU, Revolade is indicated for²:

- adult chronic ITP splenectomized patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). Revolade may be considered as second line treatment for adult non-splenectomized patients where surgery is contraindicated
- adult patients with chronic HCV infection for the treatment of thrombocytopenia, where the degree of thrombocytopenia is the main factor preventing the initiation or limiting the ability to maintain optimal interferon-based therapy

It is not known if Promacta is safe and effective in children younger than 1 year with ITP. An application was submitted to the European Medicines Agency earlier this year to include chronic ITP patients 1 year and older. This application includes chemistry, manufacturing and control data supporting the new oral suspension formulation of Promacta. The safety and efficacy profile of Promacta has not yet been established in countries outside the US in pediatric patients with chronic ITP.

Please see full Prescribing Information, including Boxed WARNING, available at <http://www.pharma.us.novartis.com/product/pi/pdf/promacta.pdf>.

MECHANISM OF ACTION

TPO receptor agonists work by inducing bone marrow stem cells to increase production of blood cells¹.

ABOUT PEDIATRIC ITP

ITP is a rare blood disorder³. It affects adults and children, including about 5 in 100,000 children each year⁴. ITP is characterized by blood that does not clot as it should due to a low number of platelets³. Blood clots help prevent bleeding and bruising following a cut or wound³. Because people with ITP have a low platelet count, they may experience bleeding that is hard to stop³.

The two types of ITP are acute (temporary or short-term) and chronic (long-lasting). Acute ITP mainly occurs in children, often after a viral infection, and generally lasts <6 months. The platelet count returns to normal within 6 to 12 months and treatment may not be needed³. Chronic ITP, which Promacta is indicated to treat, is defined as ongoing disease more than 12 months after diagnosis⁵, and it occurs in 13-36% of children with immune thrombocytopenia⁶.

ITP can occur at any time during childhood. Key symptoms³ include:

- Easy or excessive bruising
- Tiny red or purple dots on the skin
- Prolonged bleeding from cuts or wounds
- Spontaneous nose bleeds
- Bleeding gums, often during dental work

Important Safety Information for Promacta® (eltrombopag)

Promacta can cause serious side effects, including liver problems, abnormal liver function tests, high platelet counts and higher risk for blood clots, and new or worsened cataracts (a clouding of the lens in the eye).

For patients who have chronic hepatitis C virus and take Promacta with interferon and ribavirin treatment, Promacta may increase the risk of liver problems. Patients should tell a healthcare provider right away if they have any of these signs and symptoms of liver problems including yellowing of the skin or the whites of the eyes (jaundice), unusual darkening of the urine, unusual tiredness, right upper stomach area pain, confusion, swelling of the stomach area (abdomen).

A healthcare provider will order blood tests to check the liver before starting Promacta and during Promacta treatment. In some cases, treatment with Promacta may need to be stopped due to changes in liver function tests.

The risk of getting a blood clot is increased if the platelet count is too high during treatment with Promacta. The risk of getting a blood clot may also be increased during treatment with Promacta if platelet counts are normal or low. Some forms of blood clots, such as clots that travel to the lungs or that cause heart attacks or strokes can cause severe problems or death. A healthcare provider will check blood platelet counts, and change the dose of Promacta or stop Promacta, if platelet counts get too high. Patients should tell a healthcare provider right away if they have signs and symptoms of a blood clot in the leg, such as swelling, pain, or tenderness in the leg.

People with chronic liver disease may be at risk for a type of blood clot in the stomach area. Patients should tell a healthcare provider right away if they have stomach area pain that may be a symptom of this type of blood clot.

New or worsened cataracts have happened in people taking Promacta. A healthcare provider will check the patient's eyes before and during treatment with Promacta. Patients should tell a healthcare provider about any changes in eyesight while taking Promacta.



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Patients should tell a healthcare provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Promacta may affect the way certain medicines work. Certain medicines may keep Promacta from working correctly. Patients should take Promacta at least 2 hours before or 4 hours after taking products such as antacids used to treat stomach ulcers or heartburn and multivitamins or products that contain iron, calcium, aluminum, magnesium, selenium, and zinc, which may be found in mineral supplements. Patients should ask a healthcare provider if they are not sure if the medicine is one that is listed above.

Patients should avoid situations and medications that may increase the risk of bleeding while taking Promacta.

The most common side effects of Promacta when used to treat chronic ITP in adults are: nausea; diarrhea; upper respiratory tract infection (symptoms may include runny nose, stuffy nose, and sneezing); vomiting; muscle aches; urinary tract infection (symptoms may include frequent or urgent need to urinate, low fever in some people, pain or burning with urination); pain or swelling (inflammation) in the throat or mouth (oropharyngeal pain and pharyngitis); abnormal liver function tests; back pain; flu-like symptoms (influenza), including fever, headache, tiredness, cough, sore throat, and body aches; skin tingling, itching, or burning; and rash.

The most common side effects of Promacta in children 1 year and older when used to treat chronic ITP are: upper respiratory tract infections (symptoms may include runny nose, stuffy nose, and sneezing); pain or swelling (inflammation) in the nose and throat (nasopharyngitis); cough; diarrhea; fever (pyrexia); runny, stuffy nose (rhinitis); stomach (abdominal) pain; pain or swelling (inflammation) in the throat or mouth; toothache; abnormal liver function tests; rash; runny nose (rhinorrhea).

The most common side effects when Promacta is used in combination with other medicines to treat chronic HCV are: low red blood cell count (anemia); fever; tiredness; headache; nausea; diarrhea; decreased appetite; flu-like symptoms (influenza), including fever, headache, tiredness, cough, sore throat, and body aches; feeling weak; trouble sleeping; cough; itching; chills; muscle aches; hair loss; and swelling in the ankles, feet, and legs.

The most common side effects of Promacta when used to treat severe aplastic anemia are: nausea, feeling tired, cough, diarrhea, headache, pain in arms, legs, hands or feet, shortness of breath, fever, dizziness, pain in nose or throat, abdominal pain, bruising, muscle spasms, abnormal liver function tests, joint pain, and runny nose.

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

Please see full Prescribing Information, including Boxed WARNING and Medication Guide, for Promacta®.

REFERENCES:

1. Full Prescribing Information.
2. Revolade Summary of Product Characteristics.
3. What Is Immune Thrombocytopenia? National Heart, Lung and Blood Institute. Available at: <http://www.nhlbi.nih.gov/health/health-topics/topics/itp>. Accessed August 5, 2015.
4. Fogarty PF, Segal JB. The epidemiology of immune thrombocytopenic purpura. *Curr Opin Hematol*. 2007;14:515–519.
5. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386-2393.
6. George JN, Woolf SH, Raskob GE. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood*. 1996;88(1):3-40.



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