
PROMACTA[®] **CARES**[™]
(eltrombopag)

**Overview for
Healthcare Providers**

What is PROMACTA CARES?

PROMACTA CARES is a restricted distribution program that consists of a patient registry and a requirement for prescribers to complete and report baseline and periodic safety information for every patient. Prescribers, pharmacists, and patients must be enrolled in PROMACTA CARES in order to prescribe, dispense and receive PROMACTA.

This risk management program is designed to promote informed risk-benefit decisions before initiating treatment and while patients are on treatment to assure appropriate use of PROMACTA for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. PROMACTA should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding. PROMACTA should not be used in an attempt to normalize platelet counts. PROMACTA is not indicated for the treatment of thrombocytopenia due to any cause of thrombocytopenia (e.g., myelodysplasia or chemotherapy) other than chronic ITP.

PROMACTA CARES also offers optional reimbursement services to patients.

Why are medication access and medical follow-up required?

Because of certain serious risks associated with PROMACTA, PROMACTA CARES includes a registry that enrolls all patients treated with PROMACTA in order to establish the long-term safety and safe use of PROMACTA through periodic monitoring. Specifically, the registry focuses on the following risks associated with PROMACTA treatment:

- hepatotoxicity
- bone marrow reticulin formation and risk for bone marrow fibrosis
- worsened thrombocytopenia after cessation of PROMACTA leading to serious hemorrhage
- thrombotic/thromboembolic complications
- increased risk of hematological malignancies and progression of malignancy in patients with a pre-existing hematological malignancy or myelodysplastic syndrome (MDS)

Linking medication access to enrollment ensures that all patients treated with PROMACTA are monitored appropriately and evaluated every 6 months to determine if continued treatment with PROMACTA is appropriate.

Prescribers must promptly report to PROMACTA CARES any adverse events occurring in the course of the use of PROMACTA.

Prescribers must also notify PROMACTA CARES when a patient discontinues PROMACTA by completing the Patient Discontinuation and Post Therapy Follow-Up Form for PROMACTA CARES at the time of discontinuation of PROMACTA and 3 months later.

All patients who are prescribed PROMACTA are also eligible to participate in the **optional** reimbursement services support of PROMACTA CARES. This component of PROMACTA CARES can help simplify reimbursement by finding the authorized specialty pharmacy that distributes PROMACTA and has the lowest co-pay, verifying your patient's benefits and researching alternate coverage options if needed.

Overview of Steps for PROMACTA CARES

STEP

1

One-Time Prescriber Enrollment

- Prescriber enrollment is required to prescribe PROMACTA.
- Read and understand the PROMACTA PI and the requirements for PROMACTA CARES.
- Review, complete, and submit the Prescriber Enrollment Form for PROMACTA CARES.

STEP

2

Patient Enrollment

- Identify an appropriate patient for PROMACTA, educate patient on the risks and benefits of treatment with PROMACTA, make sure the patient receives the Medication Guide, instruct the patient to read it and encourage the patient to ask questions when considering PROMACTA.
- With each patient, review, complete, and submit the Patient Enrollment Form for PROMACTA CARES, answer all questions, and obtain the patient's signature on the Patient Enrollment Form for PROMACTA CARES. Keep the original, send a copy to PROMACTA CARES, and give a copy to the patient.
- Complete and submit the Patient Baseline Form for PROMACTA CARES for each patient.
- Patients must be enrolled to receive PROMACTA.

STEP

3

Patient Reimbursement Services (Optional)

- Upon enrollment, complete the Prescription and Reimbursement Services Form for PROMACTA CARES with the patient.
- PROMACTA CARES Reimbursement Consultants can answer questions about PROMACTA and reimbursement at 1-877-9-PROMACTA (1-877-977-6622).

STEP**4****Dispensing**

Pharmacies must become authorized in order to dispense PROMACTA. Pharmacies must attest to:

- Understand and comply with the requirements for PROMACTA CARES.
- Train and provide educational materials to appropriate staff responsible for prescribing and dispensing PROMACTA regarding the safe and appropriate use of PROMACTA, program monitoring requirements, program adverse event reporting requirements, and documentation requirements.
- Understand the risks associated with PROMACTA.
- Confirm the prescriber and the patient are enrolled in PROMACTA CARES with each prescription or refill by calling PROMACTA CARES at 1-877-9-PROMACTA (1-877-977-6622).
- Verify the patient is authorized to receive PROMACTA prior to dispensing each prescription/refill and record the unique prescription verification number on the Inventory Tracking Log. If a prescription verification number is not provided, PROMACTA cannot be dispensed.
- Provide the Medication Guide to the patient with each prescription/refill.
- Track and document drug distribution for each patient using the Inventory Tracking Log.
- Cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with program requirements.

Non-institutional retail pharmacies are not eligible to dispense PROMACTA.

Hospital pharmacies and physician dispensing clinics retain their preferred ordering method with PROMACTA CARES. Orders for PROMACTA are placed through the wholesaler or distributor of choice. GSK will serve as the single distributor of PROMACTA and drop ship directly to the authorized pharmacy. Once an order is received by GSK from the wholesaler or distributor, GSK will verify the pharmacy's authorization status prior to shipping.

STEP**5****Patient Support and Follow-up**

- Every 6 months, a PROMACTA CARES consultant will contact the prescriber to collect safety information and verify whether the patient should continue on PROMACTA.
- Promptly report to PROMACTA CARES any adverse events occurring during the course of the use of PROMACTA. Specifically hepatotoxicity, bone marrow reticulin formation and risk for bone marrow fibrosis, worsened thrombocytopenia after cessation of PROMACTA leading to serious hemorrhage, thrombotic/thromboembolic complications, and increased risk of hematological malignancies and progression of malignancy in patients with a pre-existing hematological malignancy or myelodysplastic syndrome (MDS).
- Notify PROMACTA CARES when a patient discontinues PROMACTA by completing the Patient Discontinuation and Post Therapy Follow-Up Form for PROMACTA CARES at the time of discontinuation of PROMACTA and 3 months later.

Fax completed forms to PROMACTA CARES at 1-866-765-0920 using the forms provided by your GlaxoSmithKline (GSK) representative, or go online to **www.PROMACTACARES.com** to download the forms.

Anytime a healthcare provider or patient has a question about PROMACTA use, risks, ITP reimbursement, or other support services, they can call PROMACTA CARES at 1-877-9-PROMACTA (1-877-977-6622).

Important Safety Information

BOXED WARNING

PROMACTA may cause hepatotoxicity. Patients receiving therapy with PROMACTA must have regular monitoring of serum liver tests (see *Laboratory Monitoring* below). Discontinue PROMACTA if ALT levels increase to $\geq 3X$ upper limit of normal (ULN) and are: progressive; or persistent for ≥ 4 weeks, or; accompanied by increased direct bilirubin; or accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation. Reinitiating treatment with PROMACTA is not recommended and should be considered only with close medical supervision and under exceptional circumstances where the potential benefit outweighs the risk.

Because of the risk for hepatotoxicity and other risks, PROMACTA is available only through a restricted distribution program called PROMACTA CARES. Under the PROMACTA CARES Program, only prescribers, pharmacies, and patients registered with the program are able to prescribe, dispense, and receive PROMACTA. To enroll in the PROMACTA CARES Program, call 1-877-9-PROMACTA.

Warnings and Precautions:

Additional safety information regarding Risk of Hepatotoxicity:

Reinitiating treatment with PROMACTA is not recommended. If the potential benefit for reinitiating PROMACTA treatment is considered to outweigh the risk for hepatotoxicity, then cautiously reintroduce PROMACTA and measure serum liver tests weekly during the dose adjustment phase. If liver tests abnormalities persist, worsen or recur, then permanently discontinue PROMACTA. Exercise caution when administering PROMACTA to patients with hepatic disease. Use a lower starting dose of PROMACTA in patients with moderate to severe hepatic disease and monitor closely.

Bone Marrow Reticulin Formation and Risk for Bone Marrow Fibrosis: PROMACTA is a thrombopoietin (TPO) receptor agonist and TPO receptor agonists increase the risk for development or progression of reticulin fibers within the bone marrow. Prior to initiation of PROMACTA, examine the peripheral blood smear closely to establish a baseline level of cellular morphologic abnormalities. Following identification of a stable dose of PROMACTA, perform CBC with WBC differential monthly. If the patient develops new or worsening morphological abnormalities or cytopenia(s), discontinue treatment with PROMACTA and consider a bone marrow biopsy, including staining for fibrosis.

Worsened Thrombocytopenia and Hemorrhage Risk After PROMACTA Cessation: Discontinuation of PROMACTA may result in thrombocytopenia of greater severity than was present prior to therapy with PROMACTA. This worsened thrombocytopenia may increase the patient's risk of bleeding, particularly if PROMACTA is discontinued while the patient is on anticoagulants or antiplatelet agents. In the controlled clinical studies, transient decreases in platelet counts to levels lower than baseline were observed following discontinuation of treatment in 10% and 6% of the PROMACTA and placebo groups, respectively. Serious hemorrhagic events requiring the use of supportive ITP medications occurred in 3 severely thrombocytopenic patients within one month following the discontinuation of PROMACTA; none were reported among the placebo group. Following discontinuation of PROMACTA, obtain weekly CBCs, including platelet counts for at least 4 weeks and consider alternative treatments for worsening thrombocytopenia, according to current treatment guidelines.

Thrombotic/Thromboembolic Complications: Thrombotic/thromboembolic complications may result from excessive increases in platelet counts. Excessive doses of PROMACTA or medication errors that result in excessive doses of PROMACTA may increase platelet counts to a level that produces thrombotic/thromboembolic complications. In the controlled clinical studies, one thrombotic/thromboembolic complication was reported within the group that received PROMACTA and none within the placebo group. Seven patients experienced thrombotic/thromboembolic complications in the extension study. Use caution when administering PROMACTA to patients with known risk factors for thromboembolism. To minimize the risk for thrombotic/thromboembolic complications, do not use PROMACTA in an attempt to normalize platelet counts. Follow the dose adjustment guidelines to achieve and maintain a platelet count of $\geq 50 \times 10^9/L$.

Malignancies and Progression of Malignancies: Stimulation of the TPO receptor on the surface of hematopoietic cells may increase the risk for hematologic malignancies. PROMACTA is not indicated for the treatment of thrombocytopenia due to causes of thrombocytopenia (eg, myelodysplasia or chemotherapy) other than chronic ITP.

Laboratory Monitoring: Complete Blood Counts (CBCs) - Monitor CBCs, including platelet counts and WBC differentials prior to initiation, throughout, and following discontinuation of PROMACTA therapy. Prior to the initiation of PROMACTA, examine the peripheral blood differential to establish the extent of red and white blood cell abnormalities. Obtain CBCs, including platelet counts and peripheral blood smears, weekly during the dose adjustment phase of therapy with PROMACTA and then monthly following establishment of a stable dose of PROMACTA. Obtain CBCs, including platelet counts, weekly for at least 4 weeks following discontinuation of PROMACTA. Liver tests: Monitor serum liver tests (ALT, AST, total and fractionated bilirubin) prior to initiation of PROMACTA, every 2 weeks during the dose adjustment phase, and monthly following establishment of a stable dose. If abnormal levels are detected, repeat the tests within 3 to 5 days. If the abnormalities are confirmed, monitor serum liver tests weekly until the abnormality(ies) resolve, stabilize, or return to baseline levels. Discontinue PROMACTA for the development of clinically important liver test abnormalities.

Cataracts: In the controlled clinical studies, cataracts developed or worsened in five patients (5%) who received 50 mg PROMACTA daily and two placebo-group patients (3%). In the extension study, cataracts developed or worsened in 4% of patients who underwent ocular examination prior to therapy with PROMACTA. Cataracts were observed in toxicology studies of eltrombopag in rodents. Perform a baseline ocular examination prior to administration of PROMACTA and, during therapy with PROMACTA, regularly monitor patients for signs and symptoms of cataracts.

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