NDA 22-291 PROMACTA® (eltrombopag)

GlaxoSmithKline

PROPOSED RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

- To promote informed risk-benefit decisions before initiating treatment and while patients are on treatment to ensure appropriate use of PROMACTA
- To establish the overall long-term safety and safe use of PROMACTA through periodic monitoring of all patients who receive PROMACTA for hepatotoxicity, bone marrow reticulin formation and risk for bone marrow fibrosis, worsened thrombocytopenia and increased hemorrhage risk after PROMACTA cessation, thrombotic/thromboembolic complications, and malignancies and progression of malignancy

II. REMS ELEMENTS

A. Medication Guide

Sponsor must provide a Medication Guide to pharmacists to be provided to patients each time PROMACTA is dispensed to increase the patient's knowledge of how to safely and effectively use PROMACTA. GSK must provide 3 copies of the Medication Guide for each unit of use bottle, in case the pharmacist dispenses less than 30 tablets from the bottle.

All authorized pharmacies must provide a Medication Guide each time they dispense PROMACTA to a patient. As part of the pharmacy authorization agreement, pharmacies must agree to provide a Medication Guide each time they dispense the drug. Please see the appended Medication Guide.

B. Elements To Assure Safe Use

1. PROMACTA will only be prescribed by healthcare providers who are specially certified under 505-1(f)(3)(A).

PROMACTA *CARES* requires prescribers to be certified and enrolled in PROMACTA *CARES* before they can prescribe PROMACTA. To become certified prescribers must complete the one-time Prescriber Enrollment Form and fax the form to PROMACTA *CARES* at 1-877-9-PROMACTA (or 1-877-977-6622). The

prescriber must receive the Prescriber Enrollment Confirmation Letter, via fax to confirm the prescriber's enrollment into PROMACTA *CARES*. To enroll, the Prescriber must attest to the following:

- I have read the full Prescribing Information for PROMACTA.
- I understand that PROMACTA is approved 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.
- I understand that PROMACTA is only indicated for use in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk of bleeding.
- I understand that PROMACTA should not be used in an attempt to normalize platelet counts.
- I understand that PROMACTA is not indicated for the treatment of thrombocytopenia due to causes of thrombocytopenia (e.g., myelodysplasia or chemotherapy) other than chronic ITP
- I understand the following risks are associated with PROMACTA:
    - PROMACTA administration may cause hepatotoxicity. If a patient develops serious liver function test abnormalities, I should discontinue treatment with PROMACTA.
    - PROMACTA increases the risk for development or progression of reticulin fibers within the bone marrow. If the patient develops new or worsening morphological abnormalities or cytopenia(s), I should discontinue treatment with PROMACTA and consider a bone marrow biopsy, including staining for fibrosis.
    - Discontinuation of PROMACTA may result in thrombocytopenia of greater severity than was present prior to therapy with PROMACTA. Serious hemorrhagic events requiring the use of supportive ITP medications occurred in clinical studies within one month following the discontinuation of PROMACTA.
    - Thrombotic/thromboembolic complications may result from excessive increases in platelet counts.
    - Stimulation by PROMACTA of the TPO receptor on the surface of hematopoietic cells may increase the risk for hematologic malignancies, especially in patients with myelodysplastic syndrome.

- I understand that each patient should be monitored as follows to assure safe use of PROMACTA:

  Complete Blood Count:

  - Monitor CBCs, including platelet counts and peripheral blood smears, prior to initiation, and weekly during the dose adjustment phase of therapy with PROMACTA.
  - Monitor CBC, including platelet counts and peripheral blood smears, monthly following establishment of a stable dose of PROMACTA.
  - If PROMACTA is discontinued, obtain CBCs, including platelet counts weekly for at least 4 weeks after discontinuation.

  Liver Tests:

  - Monitor serum liver tests (ALT, AST, bilirubin) prior to initiation of PROMACTA.
  - Monitor serum liver tests (ALT, AST, bilirubin) every 2 weeks during the dose adjustment phase and then monthly following establishment of a stable dose of PROMACTA.
  - If abnormal levels are detected, monitor serum liver tests within 3 to 5 days, then weekly until the abnormality(ies) resolve, stabilize, or return to baseline levels.
  - Discontinue PROMACTA if ALT levels increase to 3X the 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 of hepatic decompensation.

- Reinitiating treatment with PROMACTA after discontinuation due to hepatotoxicity is not recommended and should be considered only with close medical supervision and under exceptional circumstances where the potential benefit outweighs the risk. If liver test abnormalities persist, worsen or recur, then permanently discontinue PROMACTA.

- I understand that I am required to complete this Prescriber Enrollment Form to enroll (once) myself in PROMACTA *CARES.*

- I will enroll each patient by assisting in the completion of the PROMACTA *CARES* Patient Enrollment Form and completing the PROMACTA *CARES* Patient Baseline Form at the time of enrollment or within 30 days of patient enrollment. I understand that baseline data is only to be used to assess for risk factors for adverse events and to evaluate the long-term safety of PROMACTA. I will obtain the patient's signature on the Patient Enrollment Form, place the original signed form in the patient's medical record, send a copy to PROMACTA *CARES*, and give a copy to the patient.

- I will provide each patient with the Medication Guide for PROMACTA prior to providing each prescription and counsel each patient on the risks and benefits of PROMACTA.

- I will evaluate the patient's status every 6 months to determine whether the patient should continue PROMACTA, and if so, authorize treatment for another 6 months

- I will 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 complete the same again 3 months later.

- I will promptly report to PROMACTA *CARES* any adverse event occurring in the course of the use of the drug as described in the Medical and Reauthorization Form for PROMACTA *CARES.*

- I understand that it is my responsibility to ensure appropriate transition of patients to the outpatient setting if my patient(s) is initiated on PROMACTA as an inpatient.

- I understand GlaxoSmithKline (GSK), its agents, and contractors may contact me via phone, mail, or e-mail to assess the effectiveness of the program requirements for PROMACTA *CARES.*

- I understand if I fail to comply with the requirements of PROMACTA *CARES*, I may no longer be able to participate in PROMACTA *CARES.*

- I further understand that I have sole responsibility for all medical judgments and treatments, and have sole responsibility, prior to administration of PROMACTA, to counsel each patient on the risks of PROMACTA, and provide each patient with all necessary warnings concerning PROMACTA.

GSK must maintain a database of all certified prescribers in the PROMACTA *CARES* Program. GSK must monitor to ensure that only certified prescribers are prescribing PROMACTA.

GSK must monitor practitioner compliance with the certification program, including baseline data collection, the periodic safety monitoring and reauthorization, discontinuation procedure, and post-discontinuation follow-up of all patients treated with PROMACTA. If a practitioner is found to be non-compliant with the PROMACTA *CARES* Program, GSK must prevent the practitioner from prescribing PROMACTA.

Please see the following appended materials:

- Dear Prescriber/Healthcare Provider Introduction Letter
- PROMACTA *CARES* Enrollment Procedure
- PROMACTA *CARES* Compliance Monitoring Procedure
- PROMACTA *CARES* Enrollment Folder
- PROMACTA *CARES* Overview Booklet
- PROMACTA *CARES* Prescriber Enrollment Form
- PROMACTA *CARES* Prescriber Enrollment Confirmation Letter
- PROMACTA *CARES* Call Center
- PROMACTA *CARES* Instructional Video
- PROMACTA *CARES* Website (www.PROMACTA*CARES*.com)

2. PROMACTA will only be dispensed by pharmacies and healthcare settings under 505-1(f)(3)(C) (i.e., pharmacies in hospitals/institutions and physician dispensing clinics) that are specially certified under 505-1(f)(3)(B).

GSK has designed a controlled distribution system to deliver PROMACTA to select certified pharmacies including: specialty pharmacies, hospital pharmacies, and other healthcare settings (such as physician practices dispensing medication in accordance with state regulations, ambulatory treatment/infusion centers). PROMACTA will not be available to non-institutional retail pharmacies. PROMACTA will only be distributed to certified pharmacies and healthcare settings via a drop ship program through which GSK must maintain direct control over who purchases PROMACTA. The certified dispensing entity may order PROMACTA through their usual distributor; the distributor will transmit the order to the PROMACTA *CARES* Program. Please refer to the appended Controlled Distribution procedure.

- Certified pharmacies and healthcare settings can only dispense PROMACTA if they are enrolled in PROMACTA *CARES*. To enroll, the pharmacy and/or healthcare setting must complete the one-time Pharmacy Authorization and fax the form to PROMACTA *CARES* at 1-877-9-PROMACTA (or 1-877-977-6622)**.** The pharmacy and/or healthcare setting must receive a Pharmacy Authorization Confirmation Letter, via fax from the PROMACTA *CARES* to confirm that the pharmacy and/or healthcare setting is authorized to dispense PROMACTA.

To become a certified pharmacy, a recognized signatory authority for the pharmacy (e.g., pharmacy director, director of drug information, P&T Committee chair) must complete the Pharmacy Authorization Form and attest to the following:

- I understand that PROMACTA is only available through PROMACTA *CARES*. I understand that only prescribers enrolled in PROMACTA *CARES* can prescribe PROMACTA and only patients enrolled in PROMACTA *CARES* can be dispensed PROMACTA.
- I will train and provide educational materials to appropriate staff responsible for dispensing PROMACTA. The materials will address the safe and appropriate use of PROMACTA, program monitoring requirements, program adverse event reporting requirements and documentation requirements.
- I will confirm the prescriber and patient are enrolled in PROMACTA *CARES* with each prescription/refill.
- I will verify whether the patient is authorized to receive PROMACTA prior to dispensing each prescription/refill by calling 1-877-977-6622 to receive the unique prescription verification number. I will record the verification number on the Inventory Tracking Log. If a prescription verification number is not provided, PROMACTA cannot be dispensed.
- I will provide a Medication Guide each time I dispense PROMACTA.
- I will maintain and complete the Inventory Tracking Log for every prescription/refill dispensed.
- I understand that each pharmacy site is required to submit the completed Inventory Tracking Log within 10 days of the last day of each month to PROMACTA *CARES*. I will retain a copy of the Inventory Tracking Log for at least 2 years from the date of the final log entry.
- I will cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with the program requirements.

Please see the following appended materials:

- Dear Pharmacist Introduction Letter
- Dear Managed Care, Wholesaler, Distributor, and Specialty Pharmacy Customer Introduction Letter
- PROMACTA *CARES* Enrollment Procedure
- PROMACTA *CARES* Controlled Distribution Procedure
- PROMACTA *CARES* Compliance Monitoring Procedure
- Inventory Tracking Log for PROMACTA
- PROMACTA *CARES* Overview Booklet
- PROMACTA *CARES* Specialty Pharmacy Authorization Form
- PROMACTA *CARES* VA Pharmacy Authorization Form
- PROMACTA *CARES* Hospital Pharmacy and Dispensing Clinic Authorization Form
- PROMACTA *CARES* Pharmacy Authorization Confirmation Letter
- PROMACTA *CARES* Call Center
- PROMACTA *CARES* Instructional Video
- PROMACTA *CARES* Website (www.PROMACTA*CARES*.com)

3. Each patient treated with PROMACTA must be enrolled in PROMACTA *CARES* for documentation of safe-use conditions under 505-1(f)(3)(D).

The patient with the assistance of the prescriber (or healthcare provider on his/her behalf) must complete the Patient Enrollment Form and the prescriber must fax the form to PROMACTA *CARES* at 1-877-9-PROMACTA (or 1-877-977-6622). The prescriber must receive Patient Enrollment Confirmation Letter, via fax from PROMACTA *CARES* to confirm the patient's enrollment into PROMACTA *CARES*. The letter provides the unique patient ID number (PID#) assigned to the patient. Patient enrollment requires the patient to attest to the following:

- I have read and understand the Medication Guide for PROMACTA that my prescriber has given to me.
- I have asked and discussed any questions or concerns about PROMACTA or my treatment with my healthcare provider.
- I am aware that PROMACTA is associated with the following risks:
    - PROMACTA may damage my liver and cause serious illness or death. I must have blood tests to check my liver before I start taking PROMACTA and during treatment with PROMACTA.
    - Long-term use of PROMACTA may cause changes in my bone marrow. These changes may lead to abnormal blood cells or my body making less blood cells.
    - When I stop receiving PROMACTA, my low blood count may become worse than before I started receiving PROMACTA. This increases my risk for having a serious bleed. These effects are most likely to happen shortly after I stop PROMACTA or within 4 weeks of stopping PROMACTA.
    - I have a higher chance of getting a blood clot if my platelet count is too high during treatment with PROMACTA.
    - PROMACTA may worsen blood cancers and is not approved for use in patients with blood cancer or a precancerous condition called myelodysplastic syndrome (MDS).
- I will report any adverse events to my prescriber.
- I understand that I should not discontinue PROMACTA without talking to my healthcare provider.
- I understand that in order to receive PROMACTA, I am required to enroll in the risk management component of the PROMACTA *CARES* Program. My healthcare provider will monitor how I am doing on PROMACTA and report to PROMACTA *CARES* every 6 months about certain serious side effects, and make sure PROMACTA is right for me
- I understand that my healthcare provider will disclose personal and medical information about me to GlaxoSmithKline, its agents or contractors (together, "**GSK**"). Such information, to the extent permitted by applicable law, will be used by GSK and disclosed to third parties (e.g., Food and Drug Administration) in

order to better understand the safety and effectiveness of PROMACTA. Further, such information (after being de-identified of my personal information) will be used by GSK to evaluate patient enrollment in, and the administration of, PROMACTA *CARES*

- I understand that, if I do not sign this Patient Enrollment Form, I will not be enrolled in the mandatory risk management component of PROMACTA *CARES* and will not receive PROMACTA.
- I understand that GSK, its agents and contractors may contact me via phone, mail, or e-mail to survey me on the effectiveness of the program requirements for PROMACTA *CARES.*

Please see the following appended materials:

- PROMACTA *CARES* Enrollment Procedure
- PROMACTA *CARES* Patient Enrollment Form
- PROMACTA *CARES* Patient Enrollment Confirmation Letter
- PROMACTA *CARES* Patient Overview Sheet
- PROMACTA *CARES* Website (www.PROMACTA*CARES*.com)
- PROMACTA *CARES* Call Center

4. Each patient treated with PROMACTA is subject to certain monitoring under 505-1(f)(3)(E).

- Medical Follow-up –
  - Prescribers must complete a Patient Baseline Form for each patient within 30 days of enrollment and a Medical Follow-up and Authorization Form every 6 months during treatment with PROMACTA. The Medical Follow-up and Authorization Form also requires the prescriber to authorize continued treatment with PROMACTA.
  - A PROMACTA *CARES* Call Center must remind the prescriber when it is time to complete the Medical Follow-up and Authorization Form for each patient.
  - All reported serious adverse events must be further investigated and followed by the GSK Safety department. These forms can be completed and faxed to PROMACTA *CARES* at 1-877-9-PROMACTA (or 1-877-977-6622) or completed over the telephone. Please refer to the appended Long-term Monitoring Procedure.

- Patient Discontinuation – Prescriber must notify PROMACTA *CARES* when a patient discontinues PROMACTA and complete the Discontinuation and Post-Therapy Form at the time of discontinuation and 3 months later.

Please see the following appended materials:

- PROMACTA *CARES* Long-term Monitoring Procedure
- Patient Baseline Form

- Medical Follow-up and Authorization Form
- Patient Reauthorization Confirmation Letter
- Discontinuation and Post-Therapy Form
- Patient Discontinuation Letter
- Risk specific targeted follow up questionnaires
  - Bone Marrow Reticulin/Bone Marrow Fibrosis
  - Hepatobiliary Laboratory Abnormalities
  - Hematological Malignancy
  - Worsening Thrombocytopenia and Bleeding
  - Thrombotic/Thromboembolic Events
- Re-enrollment Post-Discontinuation due to Hepatotoxicity Letter #1
- Re-enrollment Post-Discontinuation due to Hepatotoxicity Letter #2
- Inventory Tracking Log for PROMACTA

C. Implementation System

The Implementation System must include the following:

- GSK must maintain a database of all certified entities including dispensing entities (i.e., pharmacies and physician dispensing clinics), and enrolled patients to monitor and evaluate implementation of the elements provided for in II.B.2. and II.B.3.
- GSK must monitor distribution of PROMACTA to determine whether the drug is only drop-shipped to certified hospitals, pharmacies, physician dispensing clinics, and patients.
- GSK must monitor certified dispensing entities to ensure only enrolled and authorized patients are receiving PROMACTA. If a dispensing entity is found to be non-compliant with the PROMACTA *CARES* Program, GSK will prevent the dispensing entity from dispensing PROMACTA.
- Based on monitoring and evaluation of these elements to assure safe use, GSK must take reasonable steps to work to improve implementation of these elements.

D. Timetable for Submission of Assessments

A REMS Assessment must be submitted to FDA every 6 months for the first 24 months following approval, then annually thereafter.

PROMACTA® CARES™
(eltrombopag)

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www.gsk.com

<<date>>

Dear Prescriber:

GlaxoSmithKline is pleased to announce the approval of PROMACTA and to introduce PROMACTA *CARES*. PROMACTA is only available through a mandatory restricted distribution program called PROMACTA *CARES*. Prescribers, pharmacists, and patients must be enrolled in PROMACTA *CARES* in order to prescribe, dispense, and receive PROMACTA.

PROMACTA is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura 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 increase the risk for bleeding. PROMACTA should not be used in an attempt to normalize platelet counts.

PROMACTA *CARES* consists of a patient registry and a requirement for prescribers to complete and report baseline and periodic safety information for every patient.

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.

All patients who are prescribed PROMACTA are also eligible to participate in the optional reimbursement services 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 research alternate coverage options if needed.

Prescriber Responsibilities for PROMACTA *CARES*

The key prescriber responsibilities are listed below and more specific details can be found on the Prescriber Enrollment Form for PROMACTA *CARES*. To prescribe, prescribers must:

- Understand the indication and risks associated with PROMACTA
- Understand and comply with the mandatory risk management program requirements of PROMACTA *CARES*

- Complete a one-time only Prescriber Enrollment Form to enroll in PROMACTA *CARES*
- Review the risk of PROMACTA outlined in the Medication Guide with each patient
- Complete a baseline evaluation for each patient
- Help each patient enroll in PROMACTA *CARES*
- Promptly report adverse events
- Fulfill monitoring requirements
- Agree to evaluate and reauthorize appropriate patients every 6 months by completing the "Medical and Reauthorization Form" for each patient
- Agree to complete the Discontinuation and Post-Therapy Form for PROMACTA *CARES* at the time of PROMACTA discontinuation and 3 months later

To enroll in PROMACTA *CARES*, complete a one time Prescriber Enrollment Form and fax it to 1-866-765-0920. You will receive a Prescriber Enrollment Confirmation Letter. Once you enroll in PROMACTA *CARES*, you do not need to enroll again. For more information contact your GlaxoSmithKline account manager, call 1-877-9-PROMACTA (1-877-966-6622) or visit www.PROMACTACARES.com.

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 ≥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 (e.g, 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.

Adverse Event Reporting

Healthcare providers should report all suspected adverse events associate with the use of PROMACTA. Please contact the GSK Response Center at 1-888-825-5249.

Please see accompanying Prescribing Information, including Medication Guide.

If you have any questions regarding the introduction of PROMACTA, please contact your GlaxoSmithKline account manager or Customer Relations at 1-800-877-1158.

Sincerely,

Michael Arning, MD, PhD
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GlaxoSmithKline
1250 South Collegeville Road
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PROMACTA® CARES™
(eltrombopag)

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<<date>>

Dear Pharmacist:

GlaxoSmithKline is pleased to announce the approval of PROMACTA and to introduce PROMACTA *CARES*. PROMACTA is only available through a mandatory restricted distribution program called PROMACTA CARES. Prescribers, pharmacists, and patients must be enrolled in PROMACTA CARES in order to prescribe, dispense, and receive PROMACTA.

PROMACTA is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura 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 increase the risk for bleeding. PROMACTA should not be used in an attempt to normalize platelet counts.

PROMACTA *CARES* consists of a patient registry and a requirement for prescribers to complete and report baseline and periodic safety information for every patient.

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.

Authorization of your pharmacy permits your pharmacy to dispense PROMACTA. It is important that you understand PROMACTA *CARES* to help your pharmacy dispense PROMACTA.

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

Pharmacy Responsibilities for PROMACTA *CARES*

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. Pharmacy authorization is a critical step of PROMACTA *CARES*. PROMACTA is available only to pharmacies that are authorized. In order to become authorized, the pharmacy must complete a Pharmacy Authorization Form and:

- Understand the risks associated with PROMACTA
- 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 and comply with the requirements for PROMACTA *CARES*
- Enroll in PROMACTA *CARES*
- Confirm the prescriber and patient are enrolled in PROMACTA *CARES* with each prescription/refill.
- 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.
- Cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with program requirements.

Fax the completed form to PROMACTA *CARES* at 1-866-765-0920. You will receive a Pharmacy Authorizations Confirmation Letter. Pharmacy authorization does not require renewal. For more information on the program, contact your GlaxoSmithKline account manager, call 1-877-9-PROMACTA (1-877-966-6622) or visit www.PROMACTACARES.com.

All patients who are prescribed PROMACTA are also eligible to participate in the optional reimbursement services of PROMACTA *CARES*. This component of PROMACTA *CARES* can help simplify reimbursement by verifying your patient's benefits and research alternate coverage options if needed.

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 ≥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 (e.g, 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.

Adverse Event Reporting

Healthcare providers should report all suspected adverse events associate with the use of PROMACTA. Please contact the GSK Response Center at 1-888-825-5249.

Please see accompanying Prescribing Information, including Medication Guide.

If you have any questions regarding the introduction of PROMACTA, please contact your GlaxoSmithKline account manager or Customer Relations at 1-800-877-1158.

Sincerely,

Michael Arning, MD, PhD
Vice President, Oncology Medicine Development Center
GlaxoSmithKline
1250 South Collegeville Road
Collegeville, PA 19426-0989

PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

<<Date>>

Dear Customer Name, *{Dear Medical Director, Dear Pharmacy Director, Dear Pharmacy Consultant, Dear Health System Provider, Wholesaler, Distributor, Direct Specialty Pharmacy, Indirect Specialty Pharmacy}*

GlaxoSmithKline is pleased to announce the approval of PROMACTA and to introduce PROMACTA *CARES*. PROMACTA is only available through a mandatory restricted distribution program called PROMACTA CARES. Prescribers, pharmacists, and patients must be enrolled in PROMACTA CARES in order to prescribe, dispense, and receive PROMACTA.

GlaxoSmithKline (GSK) is pleased to provide you with the following information regarding the supply and packaging of PROMACTA (eltrombopag) tablets.

N.D.C./SKU #	Form & Strength	Size	Wholesale Acquisition Price (WAC)	Package
0007-4640-13	Tablets 25 mg	30		Bottle
0007-4641-13	Tablets 50 mg	30		Bottle

PROMACTA is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura 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 increase the risk for bleeding. PROMACTA should not be used in an attempt to normalize platelet counts.

The PROMACTA *CARES* program consists of a patient registry and a requirement for prescribers to complete and report baseline and periodic safety information for every patient. Pharmacies must be authorized and agree to terms of use of PROMACTA before ordering.

PROMACTA will be distributed as a “drop-ship” only product. Non-institutional retail pharmacies are not eligible to dispense PROMACTA.

A DEA number is required on all PROMACTA drop-ship orders to verify pharmacy enrollment. GSK can accept and prefers EDI drop shipments for PROMACTA only. {Wholesaler, Distributor, Direct Purchasing Specialty Pharmacy} should ask their EDI contact person to coordinate electronic ordering with GSK IT.

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.

Prescriber Responsibilities for PROMACTA *CARES*

The key prescriber responsibilities are listed below and more specific details can be found on the Prescriber Enrollment Form for PROMACTA *CARES*. To prescribe, prescribers must:

- Understand the indication and risks associated with PROMACTA
- Understand and comply with the mandatory risk management program requirements of PROMACTA *CARES*
- Complete a one-time only Prescriber Enrollment Form to enroll
- Review the risks of PROMACTA in the Medication Guide with each patient
- Complete a baseline evaluation for each patient
- Help each patient enroll in PROMACTA *CARES*
- Promptly report adverse events
- Fulfill monitoring requirements
- Agree to evaluate and reauthorize appropriate patients every 6 months by completing the Medical and Reauthorization Form for each patient
- Agree to complete the Discontinuation and Post-Therapy Form for PROMACTA *CARES* at the time of PROMACTA discontinuation and 3 months later

Prescribers must complete a Prescriber Enrollment Form to enroll in PROMACTA *CARES*. Prescribers only need to enroll once.

Pharmacy Responsibilities for PROMACTA *CARES*

Pharmacy authorization is a critical step of the PROMACTA *CARES* program. PROMACTA is available only to pharmacies that are authorized. In order to become authorized, the pharmacy must:

- Understand the risks associated with PROMACTA
- Understand and comply with PROMACTA *CARES* requirements
- Enroll in PROMACTA *CARES*
- Confirm the prescriber and patient are enrolled in PROMACTA *CARES* with each prescription/refill
- 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
- Cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with program requirements
- 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

Fax the completed form to PROMACTA CARES at 1-866-765-0920. You will receive a Pharmacy Authorizations Confirmation Letter. Pharmacy authorization does not require renewal. For more information on the program, contact your GlaxoSmithKline Account Manager, call 1-877-9-PROMACTA (1-877-966-6622) or visit www.PROMACTACARES.com.

All patients who are prescribed PROMACTA are also eligible to participate in the optional reimbursement services of PROMACTA *CARES*. This component of PROMACTA *CARES* can help simplify reimbursement by verifying the patient's benefits and research alternate coverage options if needed.

Important Safety Information

BOXED WARNING

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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.

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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 (e.g, 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.

Adverse Event Reporting

Healthcare providers should report all suspected adverse events associate with the use of PROMACTA. Please contact the GSK Response Center at 1-888-825-5249.

Please see accompanying Prescribing Information, including Medication Guide.

If you have any questions about how the product is packaged or supplied, please contact me directly at {phone number} or the GSK Response Center at 1-888-825-5249.

Sincerely,

John L. Fish
Vice President
Channel Management & Pharmacy Solutions

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

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PROMACTA® CARES™
(eltrombopag)

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PROMACTA *CARES* Enrollment Folder

Specification sheet and collation order for contents

Size (h x w) inches: Flat: 12 x 18.625
Folded: 12 x 9
Capacity: .625 (5/8")

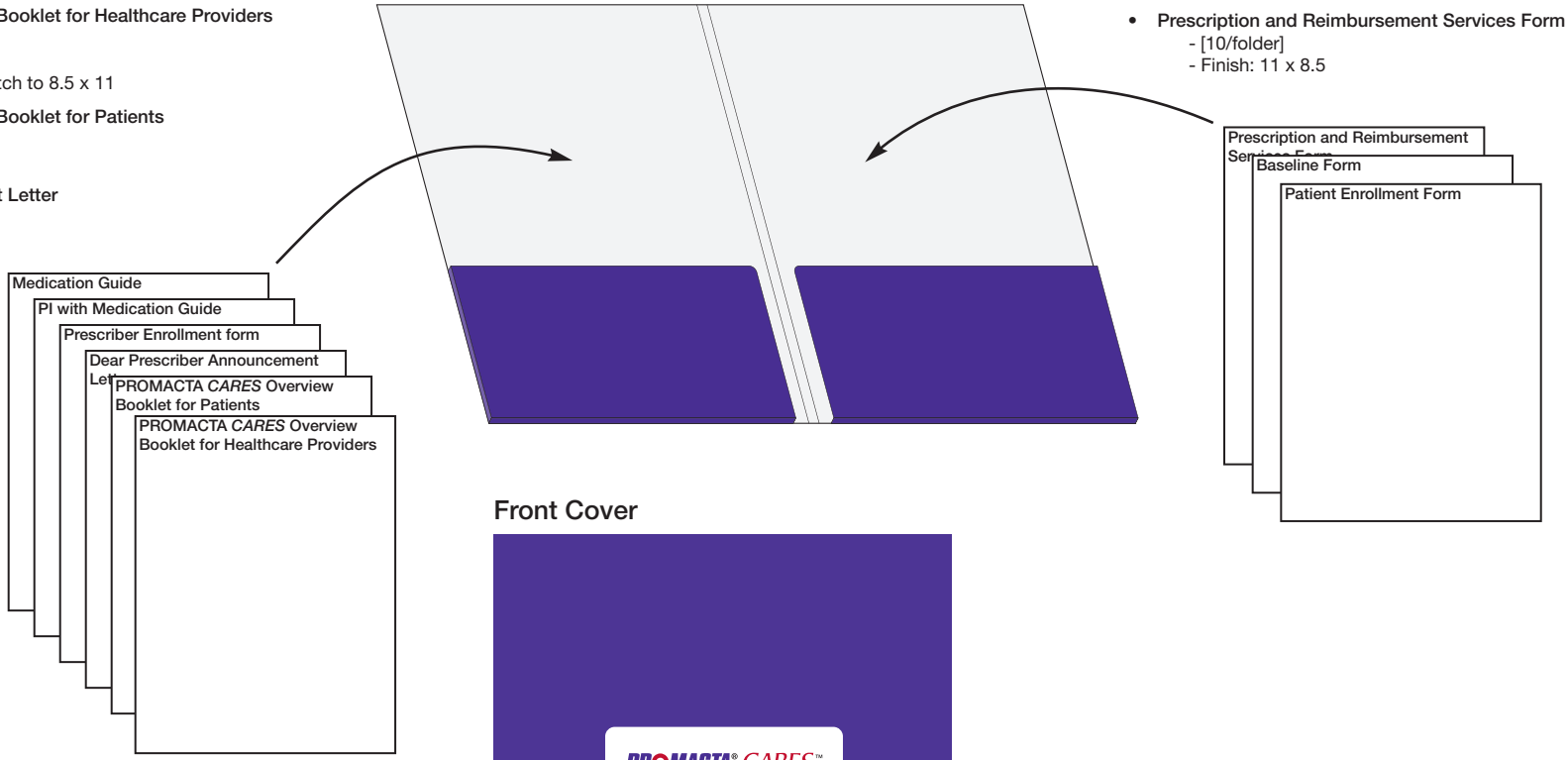
Left side [*Front to back*]

- PROMACTA *CARES* Overview Booklet for Healthcare Providers
  - [1/folder]
  - Flat:17 x 11
  - Finish: trim, score, fold, stitch to 8.5 x 11
- PROMACTA *CARES* Overview Booklet for Patients
  - [10/folder]
  - Finish: 11 x 8.5
- Dear Prescriber Announcement Letter
  - [1/folder]
  - Flat: 11 x 17
  - Finish: 11 x 8.5
- Prescriber Enrollment form
  - [1/folder]
  - Finish: 11 x 8.5
- PI with Medication Guide
  - [1 PI/folder]
  - Finish: 11 x 8.5
- Medication Guide
  - [10/folder]
  - Finish: 11 x 8.5

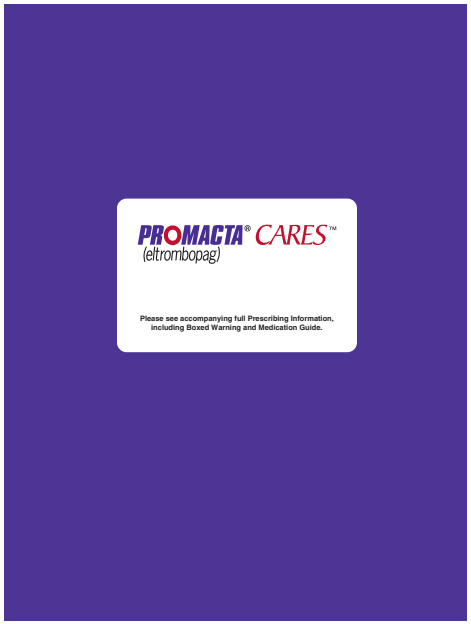
Right Side [*Front to back*]

- Patient Forms
  - Patient Enrollment Form
    - [10/folder]
    - Finish: 11 x 8.5
  - Baseline Form
    - [10/folder]
    - Finish: 11 x 8.5

  Note: These 2 forms will be shrinkwrapped together
- Prescription and Reimbursement Services Form
  - [10/folder]
  - Finish: 11 x 8.5



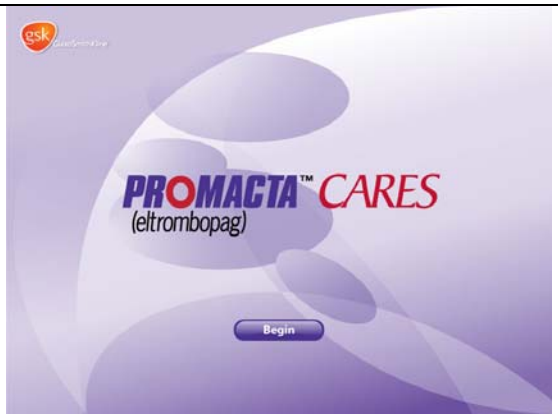
Front Cover



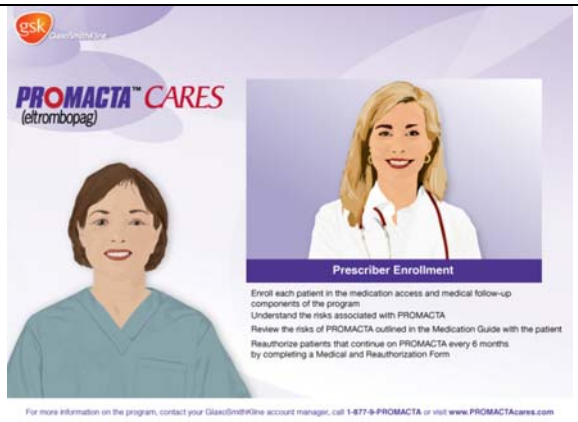
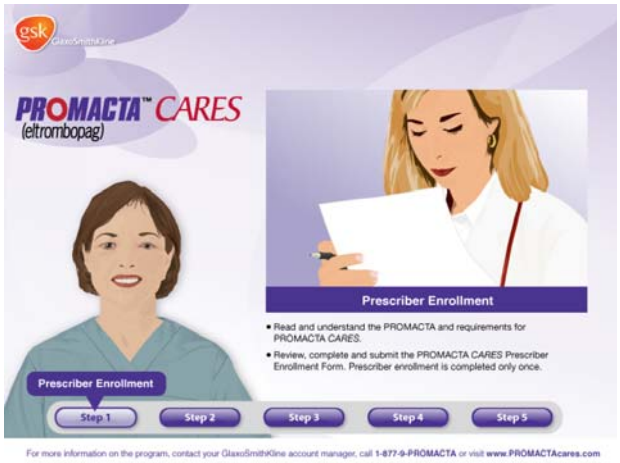
Samples of the Medical and Reauthorization Form and the Discontinuation and Post-Therapy Form will be available through GSK Account Managers and PROMACTACARES.com.

GlaxoSmithKline

PROMACTA® CARES™ (eltrombopag)

Sc #	VIDEO	AUDIO
1		
2		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 attempt to normalize platelet counts. PROMACTA is not indicated for the treatment of thrombocytopenia due to causes of thrombocytopenia other than chronic ITP. 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.
3		There are three key participants: the prescriber, pharmacy and patient . I will now discuss each participant’s role.

Sc #	VIDEO	AUDIO
4	  o Read and understand the PROMACTA PI and requirements for PROMACTA *CARES*. o Review, complete and submit the Prescriber Enrollment Form for PROMACTA *CARES*. Prescriber enrollment is completed only once. 	Here's how it works. Step 1 – Prescriber Enrollment To prescribe, prescribers must read and understand the prescribing information for PROMACTA and the requirements of PROMACTA CARES. Review and complete the Prescriber Enrollment Form. Prescriber enrollment is completed only once. The key prescriber responsibilities are listed. More specific details can be found on the Prescriber Enrollment Form for PROMACTA CARES. The Prescriber Enrollment Form is faxed to PROMACTA CARES. A confirmation of enrollment will be faxed back within one hour during business hours. Step 2 – Patient Enrollment Identify an appropriate patient for PROMACTA.

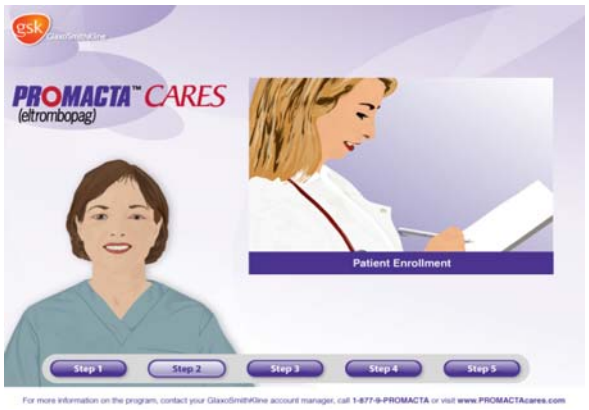
- ❑ Learn about the risks and benefits of treatment with PROMACTA described in the Medication Guide
- ❑ Enroll the patient in PROMACTA *CARES*

Educate the patient on risks and benefits of treatment with PROMACTA, and make sure the patient receives a 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. Provide a copy to the patient.

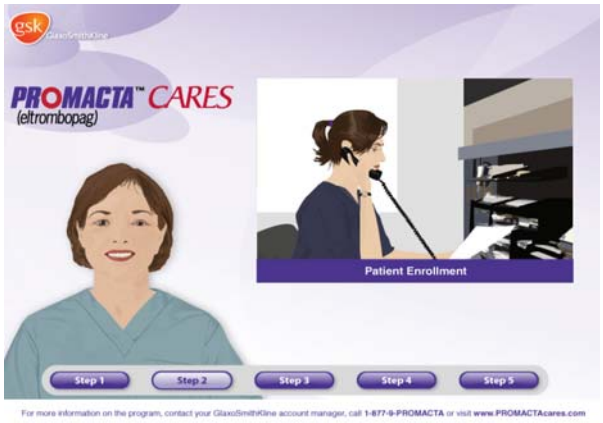
Next, complete and submit the Patient Baseline Form.

The forms are faxed to PROMACTA CARES. It is important to fill out the forms completely to avoid unnecessary delays.

Within 1 hour a unique patient ID # is faxed back to the prescriber's office.



The patient ID# should be placed in the patient's medical record. The prescriber's office may call PROMACTA CARES to obtain the patient ID # more quickly.



PROMACTA *CARES* consists of a patient registry and a requirement for prescribers to complete and report baseline and periodic safety information for every patient.

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

Patient education is a required component of the PROMACTA CARES program. PROMACTA *CARES* consists of a patient registry and a requirement for prescribers to complete and report baseline and periodic safety information for every patient.

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-

	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.	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. A PROMACTA CARES overview booklet is available to patients.
5		**Step 3 – Optional Reimbursement Services** All patients who are prescribed PROMACTA are also eligible to participate in the optional reimbursement services of PROMACTA *CARES*. There is a separate form the Prescription and Reimbursement Services Form for enrollment into the reimbursement support services. Optional reimbursement services are available to help simplify the reimbursement process for your patients. 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 research alternate coverage options if needed. Reimbursement services are available to all patients even if the prescription for PROMACTA is being filled at the prescriber's office or treatment center.

- 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 patient is enrolled in by calling PROMACTA *CARES*
- Provide the Medication Guide to the patient
- Track and document drug distribution for each patient using the Tracking Inventory Log

- The pharmacist must confirm patient enrollment and authorization status of the prescription with PROMACTA *CARES* by calling 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 patient is enrolled by calling PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622), provide the Medication Guide to the patient, track and document drug distribution for each patient using the PROMACTA Inventory Tracking Log.

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. GlaxoSmithKline (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.

Once the prescription for PROMACTA has been received at the authorized pharmacy, the pharmacist must confirm the prescriber and the patient are enrolled in PROMACTA *CARES* with each prescription or refill by calling PROMACTA *CARES* 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.

A Medication Guide is provided to the patient by the authorized dispensing pharmacy with each prescription and refill.

The pharmacist must cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with program requirements.

The form must be completed and faxed back to PROMACTA *CARES* for the patient to be reauthorized and continue on therapy beyond every 6 month interval.

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.

A Medical and Reauthorization Form is faxed to the treating prescriber every 6 months for as long as the patient continues therapy with PROMACTA. The form must be completed and faxed back to PROMACTA *CARES* for the patient to be reauthorized and to continue on therapy beyond every 6 month interval. If any of the questions are answered as “yes” or left unanswered then completion of an additional targeted follow-up questionnaire is required.

Prescribers should promptly report to PROMACTA *CARES* any adverse events occurring during the course of the use of PROMACTA.

Prescribers should notify PROMACTA *CARES* when a patient discontinues PROMACTA by completing the Discontinuation and Post Therapy Form at the time of discontinuation and approximately 3 months later.

The prescriber can acquire the form via the PROMACTA *CARES* website or by requesting PROMACTA *CARES* to fax a copy of the form to the prescriber for completion.

	 Fax completed forms to PROMACTA *CARES* at 1-866-765-0920 Visual – New Tab "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 ≥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 must promptly report to PROMACTA *CARES* any adverse events occurring in the course of the use of PROMACTA. These are critical steps for PROMACTA *CARES* in order to prescribe, dispense and receive PROMACTA. 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, reimbursement support, or other support services, they can call PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622). Audio **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 ≥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.**

	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	**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

	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	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 ≥50 x 109/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 (e.g, myelodysplasia or chemotherapy) other than chronic ITP. **Laboratory Monitoring: <u>Complete Blood Counts (CBCs)</u> -** Monitor CBCs, including platelet counts

	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 ≥50 x 109/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 (e.g, myelodysplasia or chemotherapy) other than chronic ITP. **Laboratory Monitoring: <u>Complete Blood Counts (CBCs)</u> -** 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. <u>Liver tests</u>: 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	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. <u>Liver tests</u>: 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.

	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.	

PROMACTA® CARES™
(eltrombopag)

This will link to a down-loadable version of the Prescribing Information for PROMACTA.

Print

- Home
- Prescribing Information
- Medication Guide
- To Prescribe PROMACTA
- To Dispense PROMACTA

Prescribers

To prescribe PROMACTA, click here

Pharmacies

To dispense PROMACTA, click here

This will link to a downloadable version of the Medication Guide

Home : To Prescribe PROMACTA : To Dispense PROMACTA
Resources : Download Prescribing Information : Download Medication Guide

You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

gsk GlaxoSmithKline

GSK for you
If you don't have prescription coverage and can't afford your medicines,
Visit GSKforYou.com

How may we help you?
Contact Us

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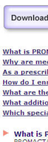
Prescribers



Prescribe - Receive - Dispense

Learn how the PROMACTA *CARES* program works. Watch this Interactive Video.

Download PROMACTA *CARES* Forms

What is PROMACTA *CARES*?
Why are medication access and medical follow-up required?
As a prescriber, how do I enroll in PROMACTA *CARES*?
How do I enroll my patients in PROMACTA *CARES*?
What are the patient support and follow-up requirements for PROMACTA *CARES*?
What additional optional program benefits are available to patients?
Which specialty pharmacies are authorized to dispense PROMACTA?

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.

As a prescriber, how do I enroll in PROMACTA *CARES*?

One-Time Prescriber Enrollment

- ☐ Prescriber enrollment is required to prescribe PROMACTA.
- ☐ Review, complete, and submit the Prescriber Enrollment Form for PROMACTA *CARES*. The form is available from the Rep@Work site, your GSK Sales Representative, or by calling PROMACTA *CARES* (1-877-977-6622).
- ☐ Fax completed forms to PROMACTA *CARES*.

PROMACTA CARES instructional video script has been submitted to Reviewing Division as separate attachments.

How do I enroll my patients in PROMACTA *CARES*?

Patient Enrollment

This links to the Resources page, from which all of the PROMACTA CARES Forms can be downloaded.

- ☐ 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.

What are the patient support and follow-up requirements for PROMACTA *CARES*?

Patient Support & Follow-up

The information outlined on this page was pulled from the section of the PROMACTA CARES Overview booklet

- ☐ Every 6 months, a PROMACTA *CARES* consultant will contact the prescriber to collect safety information and verify whether the patient should continue on PROMACTA.

  Complete and fax the Medical and Reauthorization Form for PROMACTA *CARES* to 1-866-765-0920.
- ☐ Prescribers must promptly report to PROMACTA *CARES* any adverse events occurring in 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
  - increased risk of hematological malignancies and progression of malignancy in patients with a pre-existing hematological malignancy or myelodysplastic syndrome (MDS)
- ☐ 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. Visit the Resources page to download the Medical and Reauthorization Form for PROMACTA *CARES* and the Patient Discontinuation and Post Therapy Follow-Up Form for PROMACTA *CARES*.
- ☐ 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).

What additional optional program benefits are available to patients?

All patients who are prescribed PROMACTA are eligible to participate in the optional reimbursement services of PROMACTA *CARES*.

Patient Reimbursement Services

- ☐ 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).

Which specialty pharmacies are authorized to dispense PROMACTA?

The authorized specialty pharmacies are as follows:

Clicking these links will cause the Prescriber Enrollment Form and the Resource page to open up in a new browser window.

- Accredo Health Group, Inc.
- Advanced Care Scripts
- Biologics, Inc.
- Bioscrip®
- CVS-Caremark (Pharmacare)
- CuraScript
- Diplomat
- McKesson Specialty Pharmacy / IVP Care
- OncologyRx Care Advantage
- SpecialtyScripts
- SG Bioservices
- Walgreens Specialty Pharmacy Medmark / OptionCare

The list of specialty pharmacies distributing PROMACTA is subject to change without notice, so please continue to check this site for the most complete and up-to-date list. Contact PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622) for more information about these specialty pharmacies.

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 ➢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.

Clicking here will cause the Medical and Reauthorization Form to open up in a new browser window.

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.

Clicking these 2 links will cause the Patient Discontinuation and Post Therapy Follow-up Form as well as the Resource page to open up in a new browser window.

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 ➢50 x 109/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 (e.g. myelodysplasia or chemotherapy) other than chronic ITP.

Laboratory Monitoring: Complete Blood Counts (CBCs) - Monitor CBCs, including platelet counts and WBC differential 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 starting 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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Pharmacies

Learn how the PROMACTA *CARES* program works. Watch this Interactive Video.

Download PROMACTA *CARES* Forms

What is PROMACTA *CARES*?
Why are medication access and medical follow-up required?
How does my pharmacy become authorized to dispense PROMACTA?
Which specialty pharmacies are authorized to dispense PROMACTA?

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, pharmacies, 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.

How does my pharmacy become authorized to dispense PROMACTA?

Dispensing

Pharmacies must become authorized in order to dispense PROMACTA. Pharmacies must complete the Hospital Pharmacy or Dispensing Clinic Authorization Form for PROMACTA *CARES*, Specialty Pharmacy Authorization Form for PROMACTA *CARES*, or the VA Pharmacy Authorization Form for PROMACTA *CARES* and attest to:

- ☐ Understand the risks associated with PROMACTA.
- ☐ 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, patient registration requirements, and documentation requirements.
- ☐ Confirm the prescriber and patient are enrolled in the program before dispensing prescription or refill by calling PROMACTA *CARES* (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.

PROMACTA CARES instructional video script has been submitted to Reviewing Division as separate attachments.

The Hospital Pharmacy or Dispensing Clinic Authorization Form for PROMACTA *CARES*, the Specialty Pharmacy Authorization Form for PROMACTA *CARES*, and the VA Pharmacy Authorization Form for PROMACTA *CARES* are available from the Resources page of this Web site, your GSK Sales Representative, or by calling PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622). Fax completed forms to PROMACTA *CARES* at 1-866-765-0920.

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.

This links to the Resources page, from which all of the PROMACTA CARES Forms can be downloaded.

The information outlined on this page was pulled from the section of the PROMACTA CARES Overview booklet

To become an authorized pharmacy or for more information on the program, contact your GlaxoSmithKline representative or call 1-877-9-PROMACTA (1-877-977-6622).

Which specialty pharmacies are authorized to dispense PROMACTA?

The authorized specialty pharmacies are as follows:

- Accredo Health Group, Inc.
- Advanced Care Scripts
- Biologics, Inc.
- Bioscrip®
- CVS-Caremark (Pharmacare)
- CuraScript
- Diplomat
- McKesson Specialty Pharmacy / IVP Care
- OncologyRx Care Advantage
- SpecialtyScripts
- US Bioservices
- Walgreens Specialty Pharmacy Medmark / OptionCare

The list of specialty pharmacies distributing PROMACTA is subject to change without notice, so please continue to check this site for the most complete and up-to-date list. Contact PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622) for more information about these specialty pharmacies.

Clicking any of these links will cause the Hospital Pharmacy or Dispensing Clinic Authorisation Form, the Specialty Pharmacy Authorization Form, the VA Pharmacy Authorization Form, and the Resource page to open up in a new browser window.

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 ≥ 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 ≥ 50 x 109/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 (e.g. 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 (1%) 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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Print

Resources

Prescribers/HCPs:

- Prescriber Enrollment Form
- Patient Enrollment Form
- Patient Baseline Form
- Medical and Reauthorization Form
- Discontinuation and Post-therapy Form
- Prescription and Reimbursement Services Form (optional)
- PROMACTA *CARES* Overview for Healthcare Professionals
- PROMACTA *CARES* Overview for Patients

Risk Monitoring
When you report one of these events the appropriate form from the list below will be sent to you. You can also download the form here.

- Hepatobiliary Laboratory Abnormalities
- Worsening Thrombocytopenia and Bleeding
- Hematological Malignancy
- Bone Marrow Reticulin/Bone Marrow Fibrosis
- Thrombotic and Thromboembolic Events

All REMS-related forms submitted to Reviewing Division as separate attachments.

Pharmacies:

- Hospital Pharmacy or Dispensing Clinic Authorization Form
- VA Pharmacy Authorization Form
- Specialty Pharmacy Authorization Form
- Promacta Inventory Tracking Log
  - Adobe .pdf version
  - Excel spreadsheet version
- PROMACTA *CARES* Overview for Healthcare Professionals

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PROMACTA *CARES* Enrollment Procedure

The following sections outline the procedures for:

- Prescriber Enrollment
- Pharmacy Authorization
- Patient Enrollment

Prescriber Enrollment

Prescribers (physicians and other health care professionals (HCPs) granted prescribing privileges) who wish to prescribe PROMACTA will enroll in PROMACTA *CARES* by completing the one-time Prescriber Enrollment Form. By signing the form, prescribers agree to comply with the program requirements as stated in the PROMACTA *CARES* Prescriber Enrollment Form.

Prescribers will fax the completed enrollment form to PROMACTA CARES.
The prescriber will receive a confirmation letter via fax from PROMACTA *CARES* indicating the prescriber is enrolled into PROMACTA *CARES* and authorized to prescribe PROMACTA.

A hospital or dispensing clinic pharmacy enrollment does not enroll/authorize all prescribers at an individual hospital or dispensing clinic. Therefore, each prescriber at a hospital or dispensing clinic with an authorized pharmacy must enroll in PROMACTA *CARES* in order to prescribe PROMACTA.

Pharmacy Authorization

Only authorized pharmacies will be able to dispense PROMACTA. Eligible pharmacies include specialty pharmacies, dispensing physician clinics and hospital (inpatient/outpatient) pharmacies. PROMACTA will not be available to non-institutional retail pharmacies.

Pharmacies must complete the PROMACTA *CARES* Pharmacy Authorization Form to become authorized. The signatory for the pharmacy authorization will be an individual (pharmacy director, pharmacy manager, pharmacist-in-charge, etc.) with the authority necessary to ensure that the pharmacy understands the program and has all the necessary policies and procedures in place to comply with the REMS program. By signing the form, the pharmacies agree to comply with the program requirements as stated in the PROMACTA *CARES* Pharmacy Authorization Form.

Pharmacies will fax the completed Pharmacy Authorization Form to PROMACTA CARES. The pharmacy information will then be entered into the database of authorized pharmacies. PROMACTA *CARES* will fax confirmation of authorization to the pharmacy.

Patient Enrollment

Prescriber (or an affiliated HCP) will review the benefits and risks of PROMACTA treatment as described in the Medication Guide with the patient before treatment with PROMACTA. Both, patient and prescriber will complete the PROMACTA *CARES* Patient Enrollment Form.. Patients acknowledge their review of the PROMACTA Medication Guide by signing the Patient enrollment form, agree to enroll into PROMACTA *CARES* and comply with the program requirements.

Once PROMACTA *CARES* confirms that the Patient Enrollment Form is complete, the patient will be enrolled into PROMACTA *CARES.* The patient will be assigned a unique patient identification number (PID#) which is recorded in the PROMACTA *CARES* database. During the enrollment process, PROMACTA *CARES* will determine if the patient was previously enrolled in the program. The patient maintains the same PID# for the duration of their participation in PROMACTA *CARES*; if the patient was previously enrolled, the patient will be provided the same PID# that was previously assigned. At the completion of this process, the patient will be authorized to receive PROMACTA. The patient's authorization will expire in 6 months and will require re-authorization for continued treatment.

PROMACTA *CARES* will fax the PID# to the prescriber for the purposes of including the PID# in the patients' records. The prescription does not need to include the PID# since the PID# does not change with each prescription. It will take approximately 30 minutes to 1 hour for the prescriber to receive the enrollment confirmation once the enrollment form is faxed to PROMACTA *CARES.*

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This Prescriber Enrollment Form must be completed before you can prescribe PROMACTA. PROMACTA is available only through a mandatory restricted distribution program called PROMACTA *CARES*.

I understand that PROMACTA® (eltrombopag) is only available through PROMACTA *CARES* and I agree to comply with the following program requirements:

- I have read the full Prescribing Information for PROMACTA.
- I understand that PROMACTA is approved 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.
- I understand that PROMACTA is only indicated for use in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk of bleeding.
- I understand that PROMACTA should not be used in an attempt to normalize platelet counts.
- I understand that PROMACTA is not indicated for the treatment of thrombocytopenia due to causes of thrombocytopenia (e.g., myelodysplasia or chemotherapy) other than chronic ITP.
- I understand the following risks are associated with PROMACTA:
  - PROMACTA administration may cause hepatotoxicity. If a patient develops serious liver function test abnormalities, I should discontinue treatment with PROMACTA.
  - PROMACTA increases the risk for development or progression of reticulin fibers within the bone marrow. If the patient develops new or worsening morphological abnormalities or cytopenia(s), I should discontinue treatment with PROMACTA and consider a bone marrow biopsy, including staining for fibrosis.
  - Discontinuation of PROMACTA may result in thrombocytopenia of greater severity than was present prior to therapy with PROMACTA. Serious hemorrhagic events requiring the use of supportive ITP medications occurred in clinical studies within one month following the discontinuation of PROMACTA.
  - Thrombotic/thromboembolic complications may result from excessive increases in platelet counts.
  - Stimulation by PROMACTA of the TPO receptor on the surface of hematopoietic cells may increase the risk for hematologic malignancies, especially in patients with myelodysplastic syndrome.
- I understand that each patient should be monitored as follows to assure safe use of PROMACTA:

  Complete Blood Count:
  - Monitor CBCs, including platelet counts and peripheral blood smears, prior to initiation, and weekly during the dose adjustment phase of therapy with PROMACTA.
  - Monitor CBCs, including platelet counts and peripheral blood smears, monthly following establishment of a stable dose of PROMACTA.
  - If PROMACTA is discontinued, obtain CBCs, including platelet counts weekly for at least 4 weeks after discontinuation.

  Liver Tests:
  - Monitor serum liver tests (ALT, AST, bilirubin) prior to initiation of PROMACTA.
  - Monitor serum liver tests (ALT, AST, bilirubin) every 2 weeks during the dose adjustment phase and then monthly following establishment of a stable dose of PROMACTA.
  - If abnormal levels are detected, monitor serum liver tests within 3 to 5 days, then weekly until the abnormality(ies) resolves, stabilizes, or returns to baseline levels.
  - Discontinue PROMACTA if ALT levels increase to 3X the 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 of hepatic decompensation.
- Reinitiating treatment with PROMACTA after discontinuation due to hepatotoxicity is not recommended and should be considered only with close medical supervision and under exceptional circumstances where the potential benefit outweighs the risk. If liver test abnormalities persist, worsen or recur, then permanently discontinue PROMACTA.

PROMACTA® CARES™
(eltrombopag)

continued

- I understand that I am required to complete this Prescriber Enrollment Form to enroll (once) myself in PROMACTA *CARES*.
- I will enroll each patient by assisting in the completion of the PROMACTA *CARES* Patient Enrollment Form and completing the PROMACTA *CARES* Patient Baseline Form at the time of enrollment or within 30 days of patient enrollment. I understand that baseline data is only to be used to assess for risk factors for adverse events and to evaluate the long-term safety of PROMACTA. I will obtain the patient's signature on the Patient Enrollment Form, place the original signed form in the patient's medical record, send a copy to PROMACTA *CARES*, and give a copy to the patient.
- I will provide each patient with the Medication Guide for PROMACTA prior to providing each prescription and counsel each patient on the risks and benefits of PROMACTA.
- I will evaluate the patient's status every 6 months to determine whether the patient should continue PROMACTA, and if so, authorize treatment for another 6 months.
- I will 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 complete the same again 3 months later.
- I will promptly report to PROMACTA *CARES* any adverse event occurring in the course of the use of the drug as described in the Medical and Reauthorization Form for PROMACTA *CARES*.
- I understand that it is my responsibility to ensure appropriate transition of patients to the outpatient setting if my patient(s) is initiated on PROMACTA as an inpatient.
- I understand GlaxoSmithKline (GSK), its agents, and contractors may contact me via phone, mail, or e-mail to assess the effectiveness of the program requirements for PROMACTA *CARES*.
- I understand that if I fail to comply with the requirements of PROMACTA *CARES*, I may no longer be able to participate in PROMACTA *CARES*.
- I further understand that I have sole responsibility for all medical judgments and treatments, and have sole responsibility, prior to administration of PROMACTA, to counsel each patient on the risks of PROMACTA, and to provide each patient with all necessary warnings concerning PROMACTA.

Prescriber Name (Please Print): _____

Prescriber Signature: _____ Date _____ /_____ /_____

PRESCRIBER

Prescriber Information (Please Print)

Full Name: _____ Site Name: _____

Address: _____

City: _____ State: _____ ZIP: _____

State License #: _____ State Issued: _____ DEA#: _____ NPI # (optional) _____

Specialty: _____ Phone: _____ FAX: _____ E-mail: _____

Indicate your primary treatment setting:

❑ Inpatient
❑ Outpatient facility not affiliated with an institution/hospital
❑ Outpatient facility with a dispensing clinic
❑ Outpatient facility affiliated with an institution/hospital

Should you wish to dispense from your Dispensing Clinic you must also complete the Hospital Pharmacy or Dispensing Clinic Authorization Form.

Please fax this completed form to PROMACTA *CARES* at 1-866-765-0920.

You will receive enrollment confirmation via fax within 1 hour during 8:30AM-8:00PM M-F Eastern Standard Time.

For questions regarding PROMACTA *CARES*, call 1-877-9-PROMACTA (1-877-977-6622).

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PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

<<date>>

«md_first_name» «md_last_name», «md_title»
«md_site_address2»
«md_site_city», «md_site_state» «md_site_zip»

Re: **Prescriber Enrollment Confirmation for PROMACTA *CARES***

Dear «md_first_name» «md_last_name», «md_title»:

We have received your Prescriber Enrollment Form for PROMACTA *CARES*. By enrolling in the program, you agree to comply with the program requirements outlined within the Prescriber Enrollment Form. This includes the requirement to enroll each patient who is prescribed PROMACTA.

You are now authorized to prescribe PROMACTA for your patients. PROMACTA can be accessed through the network of specialty pharmacies for PROMACTA *CARES*, **or can be dispensed at your office or treatment facility as long as they are authorized to dispense PROMACTA**. For a list of authorized pharmacy providers, visit www.PROMACTACARES.com. For information on how your Hospital Pharmacy or Dispensing Clinic can become authorized to dispense PROMACTA, please contact a GlaxoSmithKline (GSK) representative or visit www.PROMACTACARES.com.

If you have any questions, please contact us at 1-877-9-PROMACTA (1-877-977-6622). Counselors for PROMACTA *CARES* are available Monday through Friday, 8:30 AM to 8 PM Eastern Time.

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*

PROMACTA® and PROMACTA® *CARES* are trademarks of GlaxoSmithKline.

«record_id»

PROMACTA® CARES™
(eltrombopag)

Learning About PROMACTA *CARES*

An Overview for Patients

Overview of Steps for PROMACTA *CARES*

What is PROMACTA *CARES*?

PROMACTA *CARES* is a program designed to inform you about the risks and benefits of using PROMACTA. You and your healthcare provider will be able to discuss these risks and what this means for you. PROMACTA is only available through PROMACTA *CARES*.

PROMACTA *CARES* includes a registry that requires all patients treated with PROMACTA to be enrolled. Part of the registry requires that your healthcare provider monitor how you are doing on PROMACTA, to report to PROMACTA *CARES* every 6 months about certain serious side effects, and to make sure PROMACTA is right for you.

Your healthcare provider will explain the content of the Patient Enrollment Form for PROMACTA *CARES* which you must sign before receiving the medicine. After you are enrolled, you can start treatment with PROMACTA.

STEP 1 Enroll

- Your healthcare provider will explain to you what PROMACTA is and how it is used.
- Your healthcare provider will explain the risks and benefits of using PROMACTA and give you the Medication Guide for PROMACTA.
- You and your healthcare provider will fill out and sign forms once you understand the benefits and risks of PROMACTA. Once the Patient Enrollment Form is completed, you will receive a unique patient identification number from your healthcare provider.

STEP 2 Patient Reimbursement Services (Optional)

- As you enroll in PROMACTA *CARES*, you may request insurance or payment assistance. Reimbursement Specialists for PROMACTA *CARES* will work with you and look for assistance programs for which you might be eligible.
- You can call PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622) Monday through Friday 8:30am to 8pm Eastern Time to answer any of your questions about insurance or financial assistance options.

STEP 3 Receiving PROMACTA

- You will pick up PROMACTA at your hospital pharmacy, your doctor's office, or it will be delivered to your home.
- Your healthcare provider will monitor how you are doing on PROMACTA, perform blood tests to monitor your platelet count and liver function, and report any serious side effects to PROMACTA *CARES*. Therefore, the Patient Enrollment Form for PROMACTA *CARES* asks your permission to allow PROMACTA *CARES* to speak to your healthcare provider about any side effects that you might have experienced during and after therapy.
- Make sure to talk to your healthcare provider before you stop taking PROMACTA.

If you have any questions or concerns, please speak to your healthcare provider.

STEP 4 Support and Follow-up

- Reimbursement Specialists from PROMACTA *CARES* are available to answer any questions about insurance or financial assistance options.

MEDICATION GUIDE
PROMACTA® (pro-MAC-ta)
(eltrombopag)
Tablets

Read the Medication Guide that comes with PROMACTA before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about PROMACTA?
PROMACTA can cause uncommon but serious side effects:

- **Liver problems.** PROMACTA may damage your liver and cause serious illness and death. You must have blood tests to check your liver before you start taking PROMACTA and during treatment with PROMACTA. Your healthcare provider will order these blood tests. In some cases PROMACTA treatment may need to be stopped. Tell your healthcare provider 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.
- **Bone marrow changes (increased reticulin and possible bone marrow fibrosis).** Long-term use of PROMACTA may cause changes in your bone marrow. These changes may lead to abnormal blood cells or your body making less blood cells. The mild form of these bone marrow changes is called "increased reticulin". It is not known if this may progress to a more severe form called "fibrosis." The mild form may cause no problems while the severe form may cause life-threatening blood problems. Signs of bone marrow changes may show up as abnormal results in your blood tests. Your healthcare provider will decide if abnormal blood test results mean that you should have bone marrow tests or if you should stop taking PROMACTA.
- **Worsening low blood platelet count (thrombocytopenia) and risk of bleeding shortly after stopping PROMACTA.** When you stop taking PROMACTA, your low blood platelet count (thrombocytopenia) may become worse than before you started taking PROMACTA. These effects are most likely to happen within 4 weeks after you stop taking PROMACTA. The lower platelet counts during this time period may increase your risk of bleeding, especially if you take a blood thinner or other medicines that affects platelets. Your healthcare provider will check your blood platelet counts for at least 4 weeks after you stop taking PROMACTA. Call your healthcare provider right away to report any bruising or bleeding.
- **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 PROMACTA. You may have severe complications or die from some forms of blood clots, such as clots that travel to the lungs or that cause heart attacks or strokes. Your healthcare provider will check your blood platelet counts, and change your dose or stop PROMACTA if your platelet counts get too high.
- **Worsening of blood cancers.** PROMACTA is not for use in patients with blood cancer or a precancerous condition called myelodysplastic syndrome (MDS). If you have one of these conditions, PROMACTA may worsen your cancer or condition and may cause you to die sooner.

When you are being treated with PROMACTA, your healthcare provider will closely monitor your dose of PROMACTA and blood tests, including platelet counts and liver tests.

PROMACTA is available only through a program called "PROMACTA *CARES*". To receive PROMACTA, you must talk to your healthcare provider, understand the benefits and risks of PROMACTA and agree to enroll into PROMACTA *CARES*.

- During therapy with PROMACTA, your healthcare provider may change your dose of PROMACTA, depending upon the change in your blood platelet count. You must have blood platelet count tests done before, during and after your therapy with PROMACTA.
- PROMACTA is used to try to keep your platelet count about 50,000 per microliter in order to lower your risk for bleeding. PROMACTA is not used to make your platelet count normal.

See "What are the possible side effects of PROMACTA?" for other side effects of PROMACTA.

What is PROMACTA?
PROMACTA is a prescription medicine used to treat low blood platelet counts in adults with chronic immune (idiopathic) thrombocytopenic purpura (ITP), when other medicines to treat your ITP or surgery to remove the spleen have not worked well enough.

PROMACTA is only:
- prescribed by healthcare providers who are enrolled in PROMACTA *CARES*.
- given to people who are enrolled in PROMACTA *CARES*.

It is not known if PROMACTA works or if it is safe in people under the age of 18 years.
PROMACTA is for treatment of certain people with low platelet counts caused by chronic ITP, not low platelet counts caused by other conditions or diseases.

What should I tell my healthcare provider before taking PROMACTA?
Tell your healthcare provider if you:
- have liver problems
- have or had a blood clot
- have a history of cataracts
- have had surgery to remove your spleen (splenectomy)
- have a bone marrow problem, including a blood cancer or Myelodysplastic Syndrome (MDS)
- have bleeding problems
- are Asian and you are of Chinese, Japanese, Taiwanese, or Korean ancestry, you may need a lower dose of PROMACTA.
- are pregnant, think you may be pregnant, or plan to get pregnant. It is not known if PROMACTA will harm an unborn baby.

Pregnancy Registry: There is a registry for women who become pregnant during treatment with PROMACTA. If you become pregnant, consider this registry. The purpose of the registry is to collect safety information about the health of you and your baby. Contact the registry as soon as you become aware of the pregnancy, or ask your healthcare provider to contact the registry for you. You and your healthcare provider can get information and enroll in the registry by calling 1-888-825-5249.

- are breast-feeding or plan to breast-feed. It is not known if PROMACTA passes into your breast milk. You and your healthcare provider should decide whether you will take PROMACTA or breast-feed. You should not do both.

continued on next page

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal products. PROMACTA may affect the way certain medicines work. Certain other medicines may affect the way PROMACTA works. Especially tell your healthcare provider if you take:

- certain medicines used to treat high cholesterol, called "statins".
- a blood thinner medicine.

Certain medicines may keep PROMACTA from working correctly. Take PROMACTA either 4 hours before or 4 hours after taking these products:

- antacids used to treat stomach ulcers or heartburn.
- multivitamins or products that contain iron, calcium, aluminum, magnesium, selenium, and zinc which may be found in mineral supplements.

Ask your healthcare provider if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take PROMACTA?

To receive PROMACTA, you must first talk with your healthcare provider and understand the benefits and risks of PROMACTA. You must agree to and follow all of the instructions in PROMACTA *CARES*.

- Before you can begin to receive PROMACTA, your healthcare provider will:
  - explain PROMACTA *CARES* to you.
  - answer all of your questions about PROMACTA and PROMACTA *CARES*.
  - make sure you read this PROMACTA Medication Guide.
  - have you sign the PROMACTA *CARES* Patient Enrollment Form.
- Take PROMACTA exactly as your healthcare provider tells you. Do not stop using PROMACTA without talking with your healthcare provider first. Do not change your dose or schedule for taking PROMACTA unless your healthcare provider tells you to change it.
- Take PROMACTA on an empty stomach, either 1 hour before or 2 hours after eating food.
- Take PROMACTA at least 4 hours before or 4 hours after eating dairy products and calcium fortified juices.
- If you miss a dose of PROMACTA, wait and take your next scheduled dose. Do not take more than one dose of PROMACTA in one day.
- If you take too much PROMACTA, you may have a higher chance of serious side effects. Call your healthcare provider right away.
- Your healthcare provider will check your platelet count every week and change your dose of PROMACTA as needed. This will happen every week until your healthcare provider decides that your dose of PROMACTA can stay the same. After that, you will need to have blood tests every month. When you stop taking PROMACTA, you will need to have blood tests for at least 4 weeks to check if your platelet count drops too low.
- Tell your healthcare provider about any bruising or bleeding that happens while you take and after you stop taking PROMACTA.

What should I avoid while taking PROMACTA?

Avoid situations and medicines that may increase your risk of bleeding.

What are the possible side effects of PROMACTA?

PROMACTA may cause serious side effects.

- See **"What is the most important information I should know about PROMACTA?".**
- **New or worsened cataracts (a clouding of the lens in the eye).** New or worsened cataracts have happened in people taking PROMACTA. Your healthcare provider will check your eyes before and during your treatment with PROMACTA. Tell your healthcare provider about any changes in your eyesight while taking PROMACTA.

The most common side effects of PROMACTA are:

- nausea
- vomiting
- heavy or longer than normal menstrual periods
- muscle aches
- abnormal skin sensations such as tingling, itching, or burning
- indigestion
- bruising
- bleeding into the tissue that covers the eye and under side of the eyelid (conjunctiva).

These are not all the possible side effects of PROMACTA. Tell your healthcare provider if you have any side effect that bothers you or that does not go away. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store PROMACTA Tablets?

- Store at room temperature, 59ºF to 86ºF (15ºC to 30ºC).
- **Keep PROMACTA and all medicines out of the reach of children.**

What are the ingredients in PROMACTA?

Active Ingredient: eltrombopag olamine.

Inactive Ingredients:

- Tablet Core: Magnesium stearate, mannitol, microcrystalline cellulose, povidone, and sodium starch glycolate.
- Coating: Hypromellose, polyethylene glycol 400, titanium dioxide, and FD&C Yellow No. 6 aluminum lake (25 mg tablet) or FD&C Blue No. 2 aluminum lake (50 mg tablet).

General information about the safe and effective use of PROMACTA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use PROMACTA for a condition for which it was not prescribed. Do not give PROMACTA to other people even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about PROMACTA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about PROMACTA that is written for healthcare professionals. For more information you can call toll-free 1-888-825-5249.

PROMACTA is a registered trademark of GlaxoSmithKline.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

GlaxoSmithKline
Research Triangle Park, NC 27709

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Revised: November 2008
PRM:1MG

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(eltrombopag)

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Patient Enrollment Form

PROMACTA® CARES™
(eltrombopag)

This Patient Enrollment Form must be completed before you can receive PROMACTA. PROMACTA is available only through a mandatory restricted distribution program called PROMACTA *CARES*.

PATIENT

Patient Information (Please Print)

Full Name: _____

Address: _____

City: _____ State: _____ ZIP: _____ Treated In: ❑ Inpatient setting ❑ Outpatient setting

Date of birth: _____ /_____ /_____ Gender: ❑ M ❑ F Preferred Time to Contact: ❑ Day ❑ Evening

Preferred Phone: _____ Alternate Phone: _____ E-mail: _____

Patient Identification Number (Completed by the Coordinator for PROMACTA *CARES)*

#_____

PRESCRIBER

Prescriber Information (Please Print)

Treating Healthcare Provider: _____

Address: _____

City: _____ State: _____ ZIP: _____

Phone: _____ Fax: _____ E-mail: _____

Patient Acknowledgement

- I have read and understand the Medication Guide for PROMACTA that my prescriber has given to me.
- I have asked and discussed any questions or concerns about PROMACTA or my treatment with my healthcare provider.
- I am aware that PROMACTA is associated with the following risks:
  - — PROMACTA may damage my liver and cause serious illness or death. I must have blood tests to check my liver before I start taking PROMACTA and during treatment with PROMACTA.
  - — Long-term use of PROMACTA may cause changes in my bone marrow. These changes may lead to abnormal blood cells or my body making less blood cells.
  - — When I stop receiving PROMACTA, my low blood count may become worse than before I started receiving PROMACTA. This increases my risk for having a serious bleed. These effects are most likely to happen shortly after I stop PROMACTA or within 4 weeks of stopping PROMACTA.
  - — I have a higher chance of getting a blood clot if my platelet count is too high during treatment with PROMACTA.
  - — PROMACTA may worsen blood cancers and is not approved for use in patients with blood cancer or a precancerous condition called myelodysplastic syndrome (MDS).
- I will report any adverse events to my prescriber.
- I understand that I should not discontinue PROMACTA without talking to my healthcare provider.
- I understand that in order to receive PROMACTA, I am required to enroll in the risk management component of the PROMACTA *CARES* Program. My healthcare provider will monitor how I am doing on PROMACTA and report to PROMACTA *CARES* every 6 months about certain serious side effects, and make sure PROMACTA is right for me.
- I understand that my healthcare provider will disclose personal and medical information about me to GlaxoSmithKline, its agents or contractors (together, "**GSK**"). Such information, to the extent permitted by applicable law, will be used by GSK and disclosed to third parties (e.g., Food and Drug Administration) in order to better understand the safety and effectiveness of PROMACTA. Further, such information (after being de-identified of my personal information) will be used by GSK to evaluate patient enrollment in, and the administration of, PROMACTA *CARES*.
- I understand that, if I do not sign this Patient Enrollment Form, I will not be enrolled in the mandatory risk management component of PROMACTA *CARES* and will not receive PROMACTA.
- I understand that GSK, its agents and contractors may contact me via phone, mail, or e-mail to survey me on the effectiveness of the program requirements for PROMACTA *CARES*.

Patient/Guardian (Please Print): _____

Patient/Guardian Signature: _____ Date _____ /_____ /_____

Please fax this completed form to PROMACTA *CARES* at 1-866-765-0920.
You will receive enrollment confirmation via fax within 1 hour during 8:30AM-8:00PM M-F Eastern Standard Time.
For questions regarding PROMACTA *CARES*, call 1-877-9-PROMACTA (1-877-977-6622).

GlaxoSmithKline

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GlaxoSmithKline
PO Box 13398
Five Moore Drive
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North Carolina 27709

Tel. 919 483 2100
www.gsk.com

Patient ID#
DOB

<<date>>

«md_first_name» «md_last_name», «md_title»
«md_site_address2»
«md_site_city», «md_site_state» «md_site_zip»

Re: «pt_first_name» «pt_last_name»'s **Patient Enrollment Confirmation for PROMACTA *CARES***

Dear «md_first_name» «md_last_name», «md_title»:

We have received the Patient Enrollment Form for PROMACTA *CARES* that has been submitted for your patient, «pt_first_name» «pt_last_name». By enrolling into the program, your patient confirms being educated on the risks and benefits of PROMACTA and grants consent to you to complete the Patient Baseline Form for PROMACTA *CARES* and the Medical and Reauthorization Form for PROMACTA *CARES* six months post treatment initiation. In approximately six months, the Medical and Reauthorization Form for PROMACTA *CARES* will be faxed to your office and will ask questions regarding your patient's health condition during treatment with PROMACTA.

Your patient's unique patient identification number is **«record ID»**. The identification number authorizes your patient to receive PROMACTA and confirms enrollment into PROMACTA *CARES*. You should maintain the patient identification number with the patient's medical record. The patient's pharmacy provider will confirm patient enrollment with PROMACTA *CARES* prior to the distribution of PROMACTA to «pt_first_name» «pt_last_name».

PROMACTA can be accessed through the network of specialty pharmacies for PROMACTA *CARES* or can be dispensed at your office, if applicable. For a list of some of the authorized specialty pharmacy providers, visit www.PROMACTACARES.com.

If you have any questions, please contact us at <insert program phone number>. Counselors for PROMACTA *CARES* are available Monday through Friday, 8:30 AM to 8 PM Eastern Time.

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*

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«record_id»

PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

Patient ID #
DOB

<<date>>

«md_first_name» «md_last_name», «md_title»
«md_site_address2»
«md_site_city», «md_site_state» «md_site_zip»

Re: «pt_first_name» «pt_last_name»'s **Confirmation of Patient and Reimbursement Services Enrollment for PROMACTA *CARES***

Dear «md_first_name» «md_last_name», «md_title»:

We have received the Patient Enrollment Form for PROMACTA *CARES* and the Prescription and Reimbursement Services Form for PROMACTA *CARES* that have been submitted for your patient, «pt_first_name» «pt_last_name». By enrolling into the program, your patient confirms being educated on the risks and benefits of PROMACTA and grants consent to you to complete the Baseline Form for PROMACTA *CARES* and the Medical and Reauthorization Form for PROMACTA *CARES* six months post treatment initiation. In approximately six months, the Medical and Reauthorization Form will be faxed to your office and will ask questions regarding your patient's health condition during PROMACTA therapy.

Your patient's unique patient identification number is **«record ID»**. The identification number authorizes your patient to receive PROMACTA and confirms enrollment into PROMACTA *CARES*. You should maintain the patient identification number with the patient's medical record. The patient's pharmacy provider will confirm patient enrollment with PROMACTA *CARES* prior to distribution of PROMACTA to «pt_first_name» «pt_last_name».

We will review the Prescription and Reimbursement Services Form for PROMACTA *CARES* to determine the appropriate next steps to facilitate access to PROMACTA. We will contact you if any additional information is required to complete our process. After we complete our process, we will contact you to explain the outcome and future activities.

If you have any questions, please contact us at <insert program phone number>. Reimbursement counselors for PROMACTA *CARES* are available Monday through Friday, 8:30 AM to 8 PM Eastern Time.

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*

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«record_id»

PROMACTA *CARES* Program Call Center

The PROMACTA *CARES* Program includes a call center component. The call center will be staffed by PROMACTA *CARES* Consultants from a third party organization that are agents of GlaxoSmithKline. The PROMACTA *CARES* Consultants will be specifically trained on PROMACTA *CARES* Program enrollment, pharmacy authorization and safety data collection. The PROMACA *CARES* Consultants will be responsible for processing of patient and HCP enrollments and pharmacy authorizations. The PROMACTA *CARES* Consultants are also responsible for the intake and completion of the Patient Baseline Form, the Medical and Reauthorization Form, the risk-specific adverse event report forms and the Post Therapy and Discontinuation Form as well as intake of initial spontaneous adverse event reporting.

The PROMACTA *CARES* Program call center hours of operation are Monday – Friday, 8:30am to 8:00pm EST. Callers outside of these hours are instructed to leave a message that will be addressed at the beginning of the next business day. Patients calling to report an adverse event are instructed to contact their healthcare provider immediately.

Patient Baseline Form

PROMACTA® CARES™
(eltrombopag)

Patient Identification Number (Completed by the Coordinator for PROMACTA *CARES*)

#_____

PATIENT

Patient Information (Please Print)

Full Name: _____

Initials: _____ Date of birth: _____ /_____ /_____ Gender: ❑ M ❑ F

Race: ❑ Caucasian ❑ Asian ❑ Hispanic ❑ African American ❑ Other _____ ICD-9 Code: _____

Date of Enrollment in PROMACTA *CARES*: _____ /_____ /_____ Diagnosis and Date of Diagnosis _____ _____ /_____ /_____

PATIENT BASELINE INFORMATION

Previous Treatment with PROMACTA Prior to Enrollment: ❑ Yes ❑ No If Yes, from (date): _____ /_____ /_____ to _____ /_____ /_____

Baseline Platelet Count Prior to Therapy: _____ (x 10^9/L)

Splenectomy: ❑ Yes ❑ No If known, when (date): _____ /_____ /_____

Date ITP was First Diagnosed : _____ /_____ /_____ ❑ Unknown

Previous ITP Therapies:			Start Date	Stop Date				Start Date	Stop Date
Corticosteroids:	❑ Yes	❑ No	____ /____ /____	____ /____ /____	Azathioprine:	❑ Yes	❑ No	____ /____ /____	____ /____ /____
IVIg:	❑ Yes	❑ No	____ /____ /____	____ /____ /____	Cyclophosphamide	❑ Yes	❑ No	____ /____ /____	____ /____ /____
Danazol:	❑ Yes	❑ No	____ /____ /____	____ /____ /____	Other: _____			____ /____ /____	____ /____ /____
Rituximab	❑ Yes	❑ No	____ /____ /____	____ /____ /____	Other: _____			____ /____ /____	____ /____ /____
Interferon alpha	❑ Yes	❑ No	____ /____ /____	____ /____ /____	❑ Unknown				

Previous Bone Marrow Biopsy Results

❑ Yes ❑ No ❑ Report is attached
❑ Yes, not available ❑ Unknown

Previous History of Bone Marrow Abnormalities

❑ None ❑ Yes, select one or more of the following:

❑ AML ❑ CML ❑ Multiple Myeloma
❑ MDS ❑ NHL ❑ Amyloidosis
❑ ALL ❑ Hodgkins Disease ❑ Aplastic Anemia
❑ PNH ❑ Myeloproliferative Disorders ❑ Chronic Idiopathic Myelofibrosis

❑ Other, specify_____

Previous Medical History

❑ History of thromboembolic events ❑ Yes ❑ No
❑ Risk Factors for thromboembolic events ❑ Yes ❑ No
❑ History of previous malignancy ❑ Yes ❑ No
❑ Current malignancy ❑ Yes ❑ No

❑ Other, specify_____

Please Provide the Following Baseline Values:

Alanine aminotransferase (ALT) _____ Reference Range _____
Aspartate aminotransferase (AST) _____ Reference Range _____
Bilirubin _____ Reference Range _____
Alkaline Phosphatase (Alk Phos) _____ Reference Range _____

Previous History of Hepatic Abnormalities

❑ None ❑ Yes, select one or more of the following:

❑ Viral Hepatitis ❑ Autoimmune Hepatitis
❑ Alcoholic Liver Disease ❑ Gallbladder Disease
❑ Hepatic Cirrhosis

❑ Other, specify_____

Current ITP Therapies

❑ No ❑ Yes, select one or more of the following:

❑ Corticosteroids ❑ IVIg ❑ Azathioprine
❑ Rituximab ❑ Interferon alpha
❑ Cyclophosphamide ❑ Danazol

❑ Other, specify_____

REPORTER INFORMATION

	Reporter Name (Please Print)	PROMACTA Program ID # (found on enrollment confirmation fax)	Date of Report _____ /_____ /_____
❑ PROMACTA *CARES* Specialist			_____
❑ Healthcare Provider			Signature

Please fax this completed form to PROMACTA *CARES* at 1-866-765-0920.
You will receive enrollment confirmation via fax within 1 hour during 8:30AM-8:00PM M-F Eastern Standard Time.
For questions regarding PROMACTA *CARES*, call 1-877-9-PROMACTA (1-877-977-6622).

GlaxoSmithKline

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PROMACTA *CARES* Controlled Distribution Procedure

GSK has designed a controlled distribution system to deliver PROMACTA to authorized pharmacies. Only authorized pharmacies will be able to dispense PROMACTA. Eligible pharmacies include specialty pharmacies, dispensing physician clinics and hospital (inpatient/outpatient) pharmacies. PROMACTA will not be available to non-institutional retail pharmacies.

Pharmacies must complete the PROMACTA *CARES* Pharmacy Authorization Form to become authorized. Pharmacies agree to comply with the program requirements as stated by signing the PROMACTA *CARES* Pharmacy Authorization Form.

GSK will maintain the list of authorized pharmacy sites in the PROMACTA *CARES* database. Under the controlled distribution plan, a single distributor (GSK) site will ship PROMACTA to authorized pharmacies.

Pharmacies place orders for PROMACTA through their normal procurement channels. This includes wholesalers, specialty distributors or direct to GSK. Wholesalers and specialty distributors are instructed to forward the order to GSK either electronically or manually. Wholesalers and specialty distributors are not eligible to carry inventory of or distribute PROMACTA.

Controlled distribution does not imply that each wholesaler or specialty distributor will take possession of PROMACTA, it merely reflects the passing of title from one party to another in the supply chain. GSK will physically distribute PROMACTA from a single distribution point to Authorized Pharmacies ONLY. This will allow GSK to monitor/track PROMACTA shipments to the dispensing location of the Authorized Pharmacy and allow for the confirmation of the number of bottles shipped.

GSK will provide shipment authorization codes and other information to monitor shipments to authorized pharmacies and inventory levels on a monthly basis. GSK will assess orders from authorized pharmacies for completeness and compliance to the PROMACTA REMS, record the unique shipment authorization code in the PROMACTA *CARES* database and reconcile the shipping addresses against the address list of authorized pharmacies on a monthly schedule.

Specialty Pharmacies, VA Pharmacies, In-patient Hospital Pharmacies, Out-patient Hospital Pharmacies, Physician Dispensing Clinics, shall agree to maintain an Inventory Tracking Log. This log will document each instance where PROMACTA is released by the pharmacy to patients, including the number and strength of tablets dispensed along with the PROMACTA *CARES* Patient Identification Number to allow for tracking back to the patient that received the product.

Upon each dispensing the pharmacy will be required to check with PROMACTA *CARES* to confirm that the prescriber and patient are enrolled. PROMACTA *CARES* will generate a unique prescription verification number for all patients that are verified as

enrolled and supply the verification number to the pharmacy. This verification is unique to the patient (PID#) and the prescription/refill. The pharmacy will document this unique prescription verification number in the Pharmacy Inventory Tracking Log. The pharmacy will be provided the Pharmacy Inventory Tracking Log as fax or email from PROMACTA *CARES*.

The pharmacy will be required to fax the Inventory Tracking Log monthly to PROMACTA *CARES*. The dispensing information from the Inventory Tracking Log will be entered into the master product tracking system to confirm that only enrolled and active patients received the product. The pharmacy will retain its Inventory Tracking Logs for 2 years.

Authorized pharmacies will be allowed to return unused bottles of PROMACTA. Unused PROMACTA will be returned following GSK's existing policy and procedures for drug returns.

Specialty Pharmacy Authorization Form

PROMACTA® CARES™
(eltrombopag)

This Specialty Pharmacy Authorization Form must be completed before your pharmacy/pharmacies can dispense PROMACTA. PROMACTA is available only through a mandatory restricted distribution program called PROMACTA *CARES*.

Please fax this form to 1-866-765-0920. You will receive confirmation of authorization. For questions call 1-877-9-PROMACTA (1-877-977-6622).

Pharmacy Name: _____

Identification Number (Enter One):

DEA _____ NPI _____ NCPDP _____

Ship to Address: _____

City: _____ State: _____ ZIP: _____

Phone Number: _____ Fax: _____

Primary Contact: _____

E-mail: _____

Primary Wholesaler or Distributor: _____

Address: _____

City: _____ State: _____ ZIP: _____

Phone Number: _____ Fax: _____

E-mail : _____

Account #: _____

By signing below, you and all pharmacists in your dispensing clinic or pharmacy will comply with the following:

- I understand that PROMACTA is only available through PROMACTA *CARES*. I understand that only prescribers enrolled in PROMACTA *CARES* can prescribe PROMACTA and only patients enrolled in PROMACTA *CARES* can be dispensed PROMACTA.
- I will train and provide educational materials to appropriate staff responsible for dispensing PROMACTA. The materials will address the safe and appropriate use of PROMACTA, program monitoring requirements, program adverse event reporting requirements and documentation requirements.
- I will confirm the prescriber and patient are enrolled in PROMACTA *CARES* with each prescription/refill.
- I will verify whether the patient is authorized to receive PROMACTA prior to dispensing each prescription/refill by calling 1-877-977-6622 to receive the unique prescription verification number. I will record the verification number on the Inventory Tracking Log. If a prescription verification number is not provided, PROMACTA cannot be dispensed.
- I will provide a Medication Guide each time I dispense PROMACTA.
- I will maintain and complete the Inventory Tracking Log for every prescription/refill dispensed.
- I understand that each pharmacy site is required to submit the completed Inventory Tracking Log within 10 days of the last day of each month to PROMACTA *CARES*. I will retain a copy of the Inventory Tracking Log for at least 2 years from the date of the final log entry.
- I will cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with the program requirements.

_____ Authorized Pharmacy Representative Signature

_____ Date

Print Name: _____

Title: _____

Phone Number: _____ E-mail Address: _____

If you have any questions, please contact 1-877-9-PROMACTA (1-877-977-6622) or visit www.PROMACTACARES.com.

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VA Pharmacy Authorization Form

PROMACTA® CARES
(eltrombopag)

This VA Pharmacy Authorization Form must be completed before your pharmacy/pharmacies can dispense PROMACTA. PROMACTA is available only through a mandatory restricted distribution program called PROMACTA *CARES*. Please fax this form to 1-866-765-0920. You will receive confirmation of authorization. For questions call 1-877-9-PROMACTA (1-877-977-6622).

Pharmacy Name: _____

Identification Number (Enter One):

DEA _____ NPI _____ NCPDP _____

Ship to Address: _____

City: _____ State: _____ ZIP: _____

Phone Number: _____ Fax: _____

Primary Contact: _____

E-mail: _____

Primary Wholesaler or Distributor: _____

Address: _____

City: _____ State: _____ ZIP: _____

Phone Number: _____ Fax: _____

E-mail : _____

Account #: _____

Note: If you have multiple shipping sites please complete a separate authorization for each ship site.

By signing below, you and all pharmacists in your dispensing clinic or pharmacy will comply with the following:

- I understand that PROMACTA is only available through PROMACTA *CARES*. I understand that only prescribers enrolled in PROMACTA *CARES* can prescribe PROMACTA and only patients enrolled in PROMACTA *CARES* can be dispensed PROMACTA.
- I will train and provide educational materials to appropriate staff responsible for dispensing PROMACTA. The materials will address the safe and appropriate use of PROMACTA, program monitoring requirements, program adverse event reporting requirements and documentation requirements.
- I will confirm the prescriber and patient are enrolled in PROMACTA *CARES* with each prescription/refill.
- I will verify whether the patient is authorized to receive PROMACTA prior to dispensing each prescription/refill by calling 1-877-977-6622 to receive the unique prescription verification number. I will record the verification number on the Inventory Tracking Log. If a prescription verification number is not provided, PROMACTA cannot be dispensed.
- I will provide a Medication Guide each time I dispense PROMACTA.
- I will maintain and complete the Inventory Tracking Log for every prescription/refill dispensed.
- I understand that each pharmacy site is required to submit the completed Inventory Tracking Log within 10 days of the last day of each month to PROMACTA *CARES*. I will retain a copy of the Inventory Tracking Log for at least 2 years from the date of the final log entry.
- I will cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with the program requirements.

_____ Authorized Pharmacy Representative Signature

_____ Date

Print Name: _____

Title: _____

Phone Number: _____ E-mail Address: _____

If you have any questions, please contact 1-877-9-PROMACTA (1-877-977-6622) or visit www.PROMACTACARES.com.

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Hospital Pharmacy or Dispensing Clinic Authorization Form

PROMACTA® CARES™
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This Hospital Pharmacy and Dispensing Clinic Authorization Form must be completed before your pharmacy/pharmacies can dispense PROMACTA. PROMACTA is available only through a mandatory restricted distribution program called PROMACTA *CARES.*

Please fax this form to 1-866-765-0920. You will receive confirmation of authorization. For questions call 1-877-9-PROMACTA (1-877-977-6622).

Hospital Pharmacy or Dispensing Clinic Name: _____

Identification Number (Enter One):

DEA _____ NPI _____ NCPDP _____

Ship to Address: _____

City: _____ State: _____ ZIP: _____

Phone Number: _____ Fax: _____

Primary Contact: _____

E-mail: _____

Primary Wholesaler or Distributor: _____

Address: _____

City: _____ State: _____ ZIP: _____

Phone Number: _____ Fax: _____

E-mail : _____

Account #: _____

Note: If you have multiple shipping sites please complete a separate authorization for each ship site.

By signing below, you and all pharmacists in your dispensing clinic or pharmacy will comply with the following:

- I understand that PROMACTA is only available through PROMACTA *CARES*. I understand that only prescribers enrolled in PROMACTA *CARES* can prescribe PROMACTA and only patients enrolled in PROMACTA *CARES* can be dispensed PROMACTA.
- I will train and provide educational materials to appropriate staff responsible for dispensing PROMACTA. The materials will address the safe and appropriate use of PROMACTA, program monitoring requirements, program adverse event reporting requirements and documentation requirements.
- I will confirm the prescriber and patient are enrolled in PROMACTA *CARES* with each prescription/refill.
- I will verify whether the patient is authorized to receive PROMACTA prior to dispensing each prescription/refill by calling 1-877-977-6622 to receive the unique prescription verification number. I will record the verification number on the Inventory Tracking Log. If a prescription verification number is not provided, PROMACTA cannot be dispensed.
- I will provide a Medication Guide each time I dispense PROMACTA.
- I will maintain and complete the Inventory Tracking Log for every prescription/refill dispensed.
- I understand that each pharmacy site is required to submit the completed Inventory Tracking Log within 10 days of the last day of each month to PROMACTA *CARES*. I will retain a copy of the Inventory Tracking Log for at least 2 years from the date of the final log entry.
- I will cooperate with periodic audits to assure that PROMACTA is dispensed in accordance with the program requirements.

_____ Authorized Pharmacy Representative Signature

_____ Date

Print Name: _____

Title: _____

Phone Number: _____ E-mail Address: _____

If you have any questions, please contact 1-877-9-PROMACTA (1-877-977-6622) or visit www.PROMACTACARES.com.
Note: Prescribers must also be enrolled in PROMACTA *CARES* in order to prescribe PROMACTA.

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PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

<<date>>

«contact_first_name» «contact_last_name», «contact_title»
«contact_site_address2»
«contact_site_city», «contact_site_state» «contact_site_zip»

Re: **Pharmacy Authorization Confirmation for PROMACTA *CARES***

Dear «contact_first_name» «contact_last_name», «contact_title»:

We have received the Pharmacy Authorization Form for PROMACTA *CARES* from your [Specialty Pharmacy], [Hospital Pharmacy], [Dispensing Clinic] or [VA pharmacy].By enrolling in the program, you agree to comply with the program requirements outlined within the Hospital Pharmacy or Dispensing Clinic Authorization Form for PROMACTA *CARES.*

You are now authorized to order and dispense PROMACTA. Ordering and billing for PROMACTA will occur through your primary wholesaler or distributor.

If you have any questions, please contact us at 1-877-9-PROMACTA (1-877-977-6622). Counselors for PROMACTA *CARES* are available Monday through Friday, 8:30 AM to 8 PM Eastern Time.

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*

PROMACTA® and PROMACTA® *CARES* are trademarks of GlaxoSmithKline.

«record_id»

Inventory Tracking Log for PROMACTA

PROMACTA® CARES™ (eltrombopag)

From Date:

Authorized Pharmacy Name:

Address:

Contact Name: Contact Phone #:

Purchased From:			
		Quantity - 50mg tabs	Quantity - 25mg tabs
Starting Balance:			
Shipment #	Date		
Total:		0	0

Dispensing Date to Patient	Prescriber Name	*CARES* Patient ID	Rx Verification #	Med Guide Provided	Rx number	Refills Remaining	Quantity Dispensed		Dispensing Pharmacist	Total Remaining in Inventory	
							50mg	25mg		50mg	25mg
				☐						0	0
				☐						0	0
				☐						0	0
				☐						0	0
				☐						0	0
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Instructions:
The Inventory Tracking Log for PROMACTA should be faxed to PROMACTA CARES at 1-866-765-0920 within 10 days from the last day of the month.

PROMACTA *CARES* Long-term Monitoring Procedure

All patients receiving PROMACTA will be enrolled in PROMACTA *CARES* to collect information regarding their demographics, baseline status, treatment, and adverse events.

The objective is to gather, maintain, assess, and report solicited pre-defined serious adverse events (SAEs) associated with the use of PROMACTA.

Baseline

At the time of patient enrollment or within 30 days of enrollment, the prescriber will provide baseline data for every enrolled patient on the Patient Baseline Form.

The Baseline Form is a mandatory element of the PROMACTA REMS and captures the following information:

- Duration of ITP
- Baseline platelet count and liver function tests
- Previous ITP therapies and number of previous treatments
- Spleen status
- Results of any previous (baseline) bone marrow biopsies
- Previous history of any bone marrow abnormalities, MDS, hematological malignancy, hepatic abnormality, and thromboembolic events
- Concomitant ITP medication
- PROMACTA start date
- Previous treatment courses with PROMACTA

Prescribers have up to 30 days from the time of patient enrollment to complete the Baseline Form. Forms not returned 2 weeks after the enrollment of the patient will prompt follow-up with the prescriber's offices by PROMACTA *CARES* to remind them to complete the form over the telephone or by faxing the form back to PROMACTA *CARES*. This process is repeated at 3 weeks- and 4 weeks-post enrollment if the previous attempt(s) were unsuccessful.

If the Baseline Form is not returned 1 month after the patient's enrollment, the patient is no longer authorized to receive PROMACTA. The PROMACTA *CARES* database will be updated to indicate that the patient is currently ineligible to receive PROMACTA. A letter will be faxed to the prescriber for notification that the patient is no longer enrolled in PROMACTA *CARES*.

Medical Follow-up and Reauthorization

A Medical and Reauthorization Form must be filled out and returned to PROMACTA *CARES* to allow patients access to PROMACTA beyond 6 months. The rationale of this linkage is to ensure the safe use of PROMACTA through periodic re-evaluation of the patient's current medical status if treatment beyond 6 months with PROMACTA is considered. Completion of this form will be a prerequisite for continued drug access.

The Medical and Reauthorization Form is also a mechanism to actively solicit safety information. Additionally, the form will collect the information regarding the status of the patient's treatment with PROMACTA (ongoing or discontinued).

PROMACTA *CARES* will fax the Medical Follow-up and Reauthorization Form to the prescriber 5 months following patient enrollment (and every 6 months thereafter) in order to provide the prescriber sufficient time to complete the form prior to the expiration of the patient's authorization status. Information such as patient prescriber and other administrative details will be pre-populated on the form. The prescriber can also acquire the form via www.PROMACTACARES.com and return the completed form to PROMACTA *CARES* by fax or mail. Alternatively, the form can be completed by phone with a PROMACTA *CARES* representative.

Forms not returned by the expiration date of the patient's authorization will prompt follow-up with the prescriber's office by PROMACTA *CARES* to remind him/her to either complete the form over the telephone or by faxing the form to PROMACTA *CARES*. This process is repeated 1 week and 2 weeks after expiration of the patient's authorization if the previous attempt(s) were unsuccessful.

If the Medical and Reauthorization Form is not returned 15 days after the expiration of the patient's authorization, the patient is no longer authorized to receive PROMACTA. The PROMACTA *CARES* database will be updated to reflect the patient's ineligibility to receive PROMACTA and a letter will be faxed to the prescriber stating that the patient is no longer enrolled in PROMACTA *CARES*.

Once the completed Medical and Reauthorization Form is received by PROMACTA *CARES*, a Patient Reauthorization Confirmation Letter will be sent to the prescriber's office to confirm that the patient has been reauthorized with the activated PID#.

Any "yes" or "under investigation" response to any of the safety questions on the Medical and Reauthorization Form will prompt further investigation through use of risk specific targeted follow up questionnaires to maximize information on serious adverse events. The prescriber (or an affiliated HCP) will send the completed risk-specific targeted follow-up questionnaire to PROMACTA *CARES* by fax or mail. Alternatively, the form can be completed by phone with a PROMACTA *CARES* representative.

All reported serious adverse events will be followed through to resolution or final outcome.

Discontinuation and Post-therapy Follow-up Process

Prescribers (or an affiliated HCP) should notify PROMACTA *CARES* when a patient discontinues PROMACTA by completing the Discontinuation and Post-Therapy Form at the time of discontinuation and approximately 3 months later.

The form is available on the PROMACTA *CARES* website or by requesting PROMACTA *CARES* to fax a copy of the form to the prescriber. All basic information such as patient and prescriber and administrative information is pre-populated on the Form. The prescriber sends the completed form to PROMACTA *CARES* by fax, or mail. The form can also be completed by phone with a PROMACTA *CARES* representative.

Forms not returned 2 weeks after notification of the patient's discontinuation will prompt follow-up with the prescriber's office by PROMACTA *CARES* as a reminder to either complete the form over the telephone or to fax the completed form back to PROMACTA *CARES*. This process is repeated 3 weeks and 4 weeks after notification of the patient's discontinuation if the previous attempt(s) were unsuccessful. The same process is utilized to secure completion of the Discontinuation and Post-Therapy Form sent 3 months post-discontinuation.

In addition to prescriber report, PROMACTA *CARES* may become aware of patient discontinuation through a cross-check of unique prescription verification numbers allocated against currently active Patient IDs (PIDs). PROMACTA *CARES* will run a report on PIDs with no prescription verification number requests for >3 months and match this report with Post therapy and discontinuation form completions. PROMACTA *CARES* will contact (phone call) the prescriber for patients that fulfill these criteria and have not been identified as having discontinued on Post therapy and Discontinuation form to confirm their current status

Once PROMACTA *CARES* receives the notice of discontinuation, the database will be updated to reflect that the patient is no longer eligible to receive PROMACTA. A letter (Patient Discontinuation Letter to Prescribers) will be faxed to the prescriber's office as notification that the patient is no longer enrolled in PROMACTA *CARES*.

Lost to Follow-up

If a prescriber reports a patient is lost to follow-up, PROMACTA *CARES* will check the database to determine if the patient has switched to another enrolled prescriber. The database will be updated, if the patient is found to have switched to another enrolled prescriber.

Patients who are identified by the prescriber as lost to follow-up with no switch to another enrolled prescriber identified in the database will be handled in a similar manner to patients who formally discontinued PROMACTA treatment. The patient will not be contacted directly by PROMACTA *CARES*. The database will be updated to indicate that the patient will no longer be eligible to receive PROMACTA and a letter will be faxed to the prescriber for notification that the patient is no longer enrolled in PROMACTA *CARES*.

Re-enrollment

If a patient who has discontinued PROMACTA and participation in the program subsequently re-enrolls, they will be assigned their previous PID# as discussed in the Medication Access Authorization and Dispensing Process section.

There is an additional procedure for patients who previously discontinued PROMACTA due to a liver adverse event (identified as the reason for discontinuation on the Medical and Reauthorization Form or Discontinuation and Post-Therapy Form). Patients who discontinued for this reason will have this information recorded in the PROMACTA *CARES* database. If such a patient who discontinued due to an adverse liver event subsequently re-enrolls, PROMACTA *CARES* will identify their previous experience during the enrollment process. PROMACTA *CARES* will fax an alert letter (Re-enrollment Post-Discontinuation due to Hepatotoxicity Letter) along with the PID# (same as previously assigned) to the prescriber. The letter serves to alert the prescriber that this patient previously experienced a liver event that resulted in discontinuation of PROMACTA. The Re-enrollment Post-Discontinuation due to Hepatotoxicity Letter replaces the Patient Enrollment Confirmation Letter to confirm the PID# is active.

If a patient who discontinued due to an adverse liver event (hepatotoxicity) on two separate occasions (i.e. a patient who discontinued PROMACTA due to hepatotoxicity for a second time after liver tests abnormalities persisted, worsened or recurred when the patient was re-challenged with PROMACTA) subsequently re-enrolls, PROMACTA *CARES* will identify this information in the enrollment process. PROMACTA *CARES* will fax an alert letter to the prescriber (Re-enrollment Post-Discontinuation due to Hepatotoxicity with Attestation) along with the PID# (same as previously assigned) that includes an attestation for the prescriber and patient to acknowledge that they understand the risks and benefits of reinitiating PROMACTA, and that they consent to a further re-initiation of PROMACTA despite the warning in the label that PROMACTA should be "permanently discontinued" in such a situation.

Prescribers will attest to the following:

- I acknowledge that PROMACTA was previously discontinued for PATIENT PID #_____ due to hepatotoxicity.
- I acknowledge that the Prescribing Information for PROMACTA states: "**Discontinue PROMACTA if ALT levels increase to ≥3X the 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. 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."
- Based on my medical judgment, which is within my sole responsibility, I believe that the benefits associated with reinitiation of PROMACTA outweigh the risks in this circumstance.

- I have discussed with PATIENT PID #_____ such risks associated with reinitiating PROMACTA where that patient has previously discontinued PROMACTA due to hepatotoxicity.
- After a full disclosure and discussion of these risks, PATIENT PID#____has consented to reinitiation of treatment with PROMACTA.

Patients will attest to the following:

- I acknowledge that I previously stopped taking PROMACTA due to liver problems
- I acknowledge that PROMACTA may damage my liver and cause serious illness and death, and that restarting treatment with PROMACTA is not recommended.
- After discussion with my healthcare provider I understand that the possible benefits of taking PROMACTA outweigh the risks of liver problems
- I have discussed the risks of restarting PROMACTA with my doctor, and consent to restarting treatment with PROMACTA
- I understand that if I do not sign this Letter I will not be able to receive PROMACTA

Prescribers and patients will need to sign the form and fax it back to PROMACTA *CARES.*

Medical and Reauthorization Form

PROMACTA® CARES™
(eltrombopag)

PATIENT INFORMATION

Patient Information (Please print)

Full Name: _____

Date of Birth:_____/_____/_____ PROMACTA *CARES* Patient ID#: _____

Date of enrollment in PROMACTA *CARES*:_____/_____/_____ Diagnosis and date of diagnosis:_____ _____/_____/_____

ICD-9 Code: _____

Is the patient still under your care? ❑ Yes ❑ No
If NO, please provide contact information for the new prescriber, if available:_____

Do you authorize the continuation of treatment with PROMACTA for the next 6 months? ❑ Yes ❑ No

PRESCRIBER

Prescriber Information (Please print)

Full Name: _____

Phone:_____

Dear <MD Name>
Our records indicate that <patient>'s authorization to receive PROMACTA will expire on <MM/DD/YYYY> and he/she will no longer be able to receive PROMACTA. In order to prevent interrruption of <patient>'s treatment with PROMACTA, fax the completed form to_____at 1-866-765-0920 by <expiration date> and place a copy in the patient's medical record.

TREATMENT/DISCONTINUATION INFORMATION

Is the patient currently receiving PROMACTA? ❑ Yes ❑ No If YES, go to Safety Section. If NO, see below.

If "NO", Reason for Discontinuation:	If "NO", Stop Date:	If "NO", Last Dose Administered:	If "NO", Platelet Count Upon Discontinuation:
❑ Loss of response ❑ Adverse event (specify):_____ ❑ Lack of response ❑ Death: Cause of Death:_____ Date Deceased: _____/_____/_____ ❑ Lost to follow-up ❑ Other (specify):_____	_____/_____/_____	_____mg ❑ QD ❑ QOD	_____($x10^9$/L)

SAFETY INFORMATION

In the past 6 months, has the patient experienced any of the following Serious Adverse Events* not already reported to GSK?

Liver abnormality:	❑ Yes	❑ No	❑ Under Investigation
Thrombosis or thromboembolism:	❑ Yes	❑ No	❑ Under Investigation
Bone marrow reticulin:	❑ Yes	❑ No	❑ Under Investigation
Bone marrow fibrosis:	❑ Yes	❑ No	❑ Under Investigation
New hematological malignancies:	❑ Yes	❑ No	❑ Under Investigation
Progression of previously diagnosed hematological malignancies:	❑ Yes	❑ No	❑ Under Investigation

SERIOUS ADVERSE EVENTS

Has the patient experienced any additional serious adverse events in the past 6 months? ❑ Yes ❑ No

If YES, specify:_____

_____

Was the adverse event reported to GSK? ❑ Yes ❑ No

REPORTER INFORMATION

	Reporter Name/Title (Print)	Date of report: _____/_____/_____
❑ PROMACTA *CARES* Specialist		
❑ Healthcare Provider		_____ SIGNATURE

* An adverse event is SERIOUS (SAE) when the patient outcome is: 1) Death – 2) Life threatening – 3) Hospitalization – initial or prolonged – 4) Significant disability/incapacity 5) Congenital anomaly/birth defect - 6) Other (important medical events)

Please fax this completed form to PROMACTA *CARES* at 1-866-765-0920.
For questions regarding PROMACTA *CARES*, call 1-877-9-PROMACTA (1-877-977-6622).

GlaxoSmithKline

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PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

<<date>>

«md_first_name» «md_last_name», «md_title»
«md_site_address2»
«md_site_city», «md_site_state» «md_site_zip»

Re: «pt_first_name» «pt_last_name»'s «record ID» **Medical and Reauthorization Form for PROMACTA *CARES***

Dear «md_first_name» «md_last_name», «md_title»:

We have received the Medical and Reauthorization Form for PROMACTA *CARES* that has been submitted for your patient, «pt_first_name» «pt_last_name». The form indicates you have evaluated the safe use and status of your patient and determined the patient should continue PROMACTA therapy. In approximately six months, another Medical and Reauthorization Form will be faxed to your office.

If you have any questions, please contact us at 1-877-9-PROMACTA (1-877-977-6622). Counselors for PROMACTA *CARES* are available Monday through Friday, 8:30 AM to 8 PM Eastern Time.

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*

PROMACTA® and PROMACTA® *CARES* are trademarks of GlaxoSmithKline.

«record_id»

Discontinuation and Post-therapy Form

PROMACTA® CARES™
(eltrombopag)

Patient Identification Number (Completed by the Coordinator for PROMACTA *CARES*)

#_____

PATIENT

Patient Information (Please Print)

Full Name: _____

Date of Birth: _____ /_____ /_____ ☐ Male ☐ Female Date of enrollment in PROMACTA *CARES*: _____ /_____ /_____

Diagnosis and date of diagnosis: _____

ICD-9 Code: _____ Is the patient still under your care? ☐ Yes ☐ No

If NO, please provide contact information for the new prescriber, if available:

Name: _____ Phone: _____

PRESCRIBER

Prescriber Information (Please Print)

First Name: _____ Last Name: _____

Phone: _____

PROMACTA Treatment Information

Start Date: _____ /_____ /_____ Last Dose Received: _____ mg ☐ QD ☐ QOD

Stop Date: _____ /_____ /_____ Platelet Count Upon Discontinuation: ____ (x 10^9/L)

Reason for Discontinuation:

☐ Loss of response ☐ Adverse event (specify): _____

☐ Lack of response ☐ Death: Cause of Death: _____

Date Deceased: _____ /_____ /_____

☐ Lost to follow-up ☐ Other (specify): _____

Safety Information

Did any of the following Serious Adverse Events* occur with the discontinuation of PROMACTA?

After stopping PROMACTA, did the patient experience any bleeding event requiring hospitalization or medical intervention because the platelet count worsened below baseline levels?	☐ Yes	☐ No	☐ Under Investigation Date of onset: _____ /_____ /_____
Liver abnormality	☐ Yes	☐ No	☐ Under Investigation Date of onset: _____ /_____ /_____
Thrombosis or thromboembolism	☐ Yes	☐ No	☐ Under Investigation Date of onset: _____ /_____ /_____
Bone marrow reticulin formation	☐ Yes	☐ No	☐ Under Investigation Date of onset: _____ /_____ /_____
Bone marrow fibrosis	☐ Yes	☐ No	☐ Under Investigation Date of onset: _____ /_____ /_____

* An adverse event is SERIOUS (SAE) when the patient outcome is: 1) Death – 2) Life threatening – 3) Hospitalization – initial or prolonged – 4) Significant disability/incapacity 5) Congenital anomaly/birth defect - 6) Other (important medical events)

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(eltrombopag)

Safety Information

Did any of the following Serious Adverse Events* occur with the discontinuation of PROMACTA?

Hematological malignancy ☐ Yes ☐ No ☐ Under Investigation

If Yes, then describe: _____

☐ Progression of previously diagnosed disease

☐ New onset

Date of onset: _____ /_____ /_____

Post-Therapy Follow-up

Since the report of discontinuation, what is the status of the event(s)?

Event _____ ☐ stabilized ☐ improved ☐ ongoing ☐ worsened ☐ resolved

If stabilized/improved/resolved: Date: _____ /_____ /_____

Event _____ ☐ stabilized ☐ improved ☐ ongoing ☐ worsened ☐ resolved

If stabilized/improved/resolved: Date: _____ /_____ /_____

Event _____ ☐ stabilized ☐ improved ☐ ongoing ☐ worsened ☐ resolved

If stabilized/improved/resolved: Date: _____ /_____ /_____

Event _____ ☐ stabilized ☐ improved ☐ ongoing ☐ worsened ☐ resolved

If stabilized/improved/resolved: Date: _____ /_____ /_____

Reporter Information

Reporter Name/Title (Print)

☐ PROMACTA *CARES* Specialist

☐ Prescriber

Date of report:

_____ /_____ / _____
(MM/DD/YY)

_____
Signature

* An adverse event is SERIOUS (SAE) when the patient outcome is: 1) Death – 2) Life threatening – 3) Hospitalization – initial or prolonged – 4) Significant disability/incapacity 5) Congenital anomaly/birth defect - 6) Other (important medical events)

Please fax this completed form to PROMACTA *CARES* at 1-866-765-0920.

You will receive enrollment confirmation via fax within 1 hour during 8:30AM-8:00PM M-F Eastern Standard Time.

For questions regarding PROMACTA *CARES*, call 1-877-9-PROMACTA (1-877-977-6622).

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PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

<<date>>

«md_first_name» «md_last_name», «md_title»
«md_site_address2»
«md_site_city», «md_site_state» «md_site_zip»

Re: «pt_first_name» «pt_last_name»'s PROMACTA *CARES* discontinuation

Dear «md_first_name» «md_last_name», «md_title»:

This letter is to inform you that your patient, «pt_first_name» «pt_last_name», has been discontinued from PROMACTA *CARES* and his/her patient ID_____ is no longer active. Please note that another Discontinuation and Post-therapy Form will be sent to you for completion.

If you have any questions, please contact PROMACTA *CARES* at 1-877-9-PROMACTA

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*

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«record_id»

PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

<<date>>

«md_first_name» «md_last_name», «md_title»
«md_site_address2»
«md_site_city», «md_site_state» «md_site_zip»

Re: «pt_first_name» «pt_last_name»'s («record ID») **Previous Discontinuation Due to Hepatotoxicity**

Dear «md_first_name» «md_last_name», «md_title»:

This is to inform you that Patient «pt_first_name» «pt_last_name» PID #_____discontinued treatment with PROMACTA on [Date of Discontinuation] due to hepatotoxicity.

For additional information about the circumstances of this patient's discontinuation please call PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622).

The Prescribing Information for PROMACTA states:

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. If liver tests abnormalities persist, worsen or recur, then permanently discontinue PROMACTA.

WARNING: RISK FOR HEPATOTOXICITY

See full prescribing information for complete boxed warning.

PROMACTA may cause hepatotoxicity:

- **Measure serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin prior to initiation of PROMACTA, every 2 weeks during the dose adjustment phase, and monthly following establishment of a stable dose. If bilirubin is elevated, perform fractionation.**
- **Evaluate abnormal serum liver tests with repeat testing 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 if ALT levels increase to ≥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.**

The Patient ID# ____ has been activated.

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*

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«record_id»

PROMACTA® CARES™
(eltrombopag)

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

Tel. 919 483 2100
www.gsk.com

<<date>>

«md_first_name» «md_last_name», «md_title»
«md_site_address2»
«md_site_city», «md_site_state» «md_site_zip»

Re: Patient Name and DOB

Dear «md_first_name» «md_last_name», «md_title»:

This is to inform you that your Patient, PID #_____, discontinued treatment with PROMACTA on ***[Dates of Discontinuation]*** because of hepatotoxicity.

For additional information about the circumstances of this patient's discontinuation please call PROMACTA *CARES* at 1-877-9-PROMACTA (1-877-977-6622).

GlaxoSmithKline (GSK) writes to remind you that the Prescribing Information for PROMACTA states:

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.

WARNING: RISK FOR HEPATOTOXICITY

PROMACTA may cause hepatotoxicity:

- **Measure serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin prior to initiation of PROMACTA, every 2 weeks during the dose adjustment phase and monthly following establishment of a stable dose. If bilirubin is elevated, perform fractionation.**
- **Evaluate abnormal serum liver tests with repeat testing 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 if ALT levels increase to ≥3X the 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.**

Because of the risk for hepatotoxicity and other risks *[see Warnings and Precautions (5.1-5.6)]*, PROMACTA is available only through a restricted distribution program called PROMACTA *CARES*. Under PROMACTA *CARES*, only prescribers, pharmacies, and patients registered with the program are able to prescribe, dispense, and receive PROMACTA. To enroll in PROMACTA *CARES*, call 1-877-9-PROMACTA *[see Warnings and Precautions (5.8)]*.

Please acknowledge the following and sign below:

- I acknowledge that PROMACTA was previously discontinued for PATIENT PID #_____ due to hepatotoxicity.
- I acknowledge that the Prescribing Information for PROMACTA states: "**Discontinue PROMACTA if ALT levels increase to ≥3X the 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. 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."
- Based on my medical judgment, which is within my sole responsibility, I believe that the benefits associated with reinitiation of PROMACTA outweigh the risks in this circumstance.
- I have discussed with PATIENT PID #_____ such risks associated with reinitiating PROMACTA where that patient has previously discontinued PROMACTA due to hepatotoxicity.
- After a full disclosure and discussion of these risks, PATIENT PID#_____ has consented to reinitiation of treatment with PROMACTA.

_____ _____

Prescriber Signature Date

Please have your Patient acknowledge and sign below:

- I acknowledge that I previously stopped taking PROMACTA due to liver problems.
- I acknowledge that PROMACTA may damage my liver and cause serious illness and death, and that restarting treatment with PROMACTA is not recommended.
- After discussion with my healthcare provider I understand that the possible benefits of taking PROMACTA outweigh the risks of liver problems.
- I have discussed the risks of restarting PROMACTA with my doctor, and consent to restarting treatment with PROMACTA.
- I understand that if I do not sign this Letter I will not be able to receive PROMACTA.

_____ _____

Patient Signature Date

Please send this signed letter to PROMACTA *CARES* via fax 866-765-0920.

If you have any questions, please contact us at 1-877-9-PROMACTA (1-877-977-6622). Counselors for PROMACTA *CARES* are available Monday through Friday, 8:30 AM to 8 PM Eastern Time.

Sincerely,

«user_first_name» «user_last_name»
PROMACTA *CARES*
PROMACTA® and PROMACTA® *CARES* are trademarks of GlaxoSmithKline.

«record_id»

GlaxoSmithKline

Promacta® (eltrombopag)
Bone Marrow Reticulin / Bone Marrow Fibrosis

Section 1. Patient Information

Initials:	**PROMACTA *CARES* ID:**	**OCEANS Case No:** (For GSK use only)
Age:	**Date of Birth:** ____ / ____ / _____ (mm / dd / yyyy)	**Gender:** ☐ Male ☐ Female

Section 2. Promacta Therapy

Date when Promacta was started: ____ / ____ / _____ (mm / dd / yyyy)	**Is the patient still taking Promacta?** ☐ Yes ☐ No	**If YES, what was the dose of Promacta at the time of the event?** _____mg **If NO, what were the last dose and the date?** _____mg **Date:** ____ / ____ / _____ (mm / dd / yyyy)

Section 3. Adverse Event

Please indicate which adverse event is being assessed. ☐ Bone marrow reticulin ☐ Bone marrow fibrosis

Date of this event: ____ / ____ / _____ (mm / dd / yyyy)

Is the bone marrow biopsy consistent with the diagnosis of ITP? ☐ Yes ☐ No

Is this a serious adverse event? ☐ Yes ☐ No

If YES, please indicate the seriousness criteria below:

- ☐ Death
- ☐ Hospitalization – initial or prolonged
- ☐ Congenital anomaly/birth defect
- ☐ Life-threatening
- ☐ Persistent or significant disability/incapacity
- ☐ Other, (important medical events)_____

Outcome of the event:

- ☐ Resolved
- ☐ Resolving/recovering
- ☐ Resolved with sequelae
- ☐ Not resolved

Is this event related to treatment with Promacta? ☐ Yes ☐ No

Was the Peripheral Blood Smear Abnormal? ☐ Yes ☐ No **Date of this smear:** ____ / ____ / ____ (mm / dd / yyyy)

If YES, were any of the following cells present in the peripheral blood smear?

Yes	No		
☐	☐	Increased peripheral blast cells	Please provide the % _____
☐	☐	Increased nucleated red blood cells	Please provide the % _____
☐	☐	Tear drop erythrocytes	

Bone marrow aspirate	☐ Yes ☐ No	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ Yes ☐ No **If YES, please specify:**
Bone marrow biopsy	☐ Yes ☐ No	____ / ____ / _____ (mm / dd / yyyy)	**Silver stain:** ☐ Done ☐ Not done **Results:**_____ **Trichrome stain:** ☐ Done ☐ Not done **Results:**
Immunophenotype	☐ Yes ☐ No	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ Yes ☐ No **If YES, please specify:**
Cytogenetics	☐ Yes ☐ No	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ Yes ☐ No **If YES, please specify:**

What clinical features were present at the time of the event? (check all that apply)

- ☐ Recent decrease in hemoglobin
- ☐ Recent decrease in platelet counts
- ☐ Increased nucleated red blood cells
- ☐ Change in white blood cells, (please specify) _____
- ☐ Newly diagnosed splenomegaly
- ☐ Newly diagnosed hepatomegaly
- ☐ Other (please specify) _____

Please quantify the degree of bone marrow reticulin/collagen using the Bauermeister scale. (Select only one)

- 0 ☐ **No reticulin fibers demonstrable**
- 1 ☐ **Occasional fine individual fibers and foci of a fine fiber network**
- 2 ☐ **Fine fiber network throughout most of the section; no coarse fibers**
- 3 ☐ **Diffuse fiber network with scattered thick coarse fibers but no mature collage** (negative trichrome stain)
- 4 ☐ **Diffuse, often coarse fiber network with areas of collagenization** (positive trichrome stain)
- ☐ **Other (please describe)** _____

You may attach anonymized copy of the bone marrow report, if available. ☐ **Check this box if attached**

Section 4. Medical History - Baseline Assessments

Please complete baseline information on any of the assessments below indicating that any of the following procedures were performed prior to the patient being treated with Promacta?

Bone marrow aspirate	☐**Yes** ☐**No**	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ **Yes** ☐**No** **If YES, please specify:**
Bone marrow biopsy	☐**Yes** ☐**No**	____ / ____ / _____ (mm / dd / yyyy)	**Silver stain:** ☐**Done** ☐**Not done** **Results:**_____ **Trichrome stain**: ☐**Done** ☐**Not done** **Results:**
Immunophenotype	☐**Yes** ☐**No**	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ **Yes** ☐**No** **If YES, please specify:**
Cytogenetics	☐**Yes** ☐**No**	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ **Yes** ☐**No** **If YES, please specify:**

At baseline, please quantify the degree of bone marrow reticulin/collagen using the Bauermeister scale. (Select only 1)

- 0 ☐ **No reticulin fibers demonstrable**
- 1 ☐ **Occasional fine individual fibers and foci of a fine fiber network**
- 2 ☐ **Fine fiber network throughout most of the section; no coarse fibers**
- 3 ☐ **Diffuse fiber network with scattered thick coarse fibers but no mature collage** (negative trichrome stain)
- 4 ☐ **Diffuse, often coarse fiber network with areas of collagenization** (positive trichrome stain)
- ☐ **Other (please describe)** _____

You may attach anonymized copy of the bone marrow report, if available. ☐ **Check this box if attached**

Section 5. Medical Information

Has the patient received radiation therapy prior to being treated with Promacta? ☐**Yes** ☐**No** ☐**Unknown**

If YES, please specify the body site:

Please indicate any concomitant medications? (check all that apply)

- ☐ **None**
- ☐ **Azathioprine**
- ☐ **Corticosteroids**
- ☐ **Cyclophosphamide**
- ☐ **Danazol**
- ☐ **Interferon alpha**
- ☐ **IVIg**
- ☐ **Rituximab**
- ☐ **Other** (please specify):_____

Please list previous and concurrent disease(s)

☐ **None**

Section 6. Reporter

- ☐ **PROMACTA *CARES* specialist** **Name and Title** _____
- ☐ **Healthcare Provider** **Name and Title** _____
- ☐ **Institution** **Name and Title** _____
- ☐ **Other (specify)** _____ **Name and Title** _____

smsq

Date of this report ____ / ____ / _____ **Signature**_____
(mm / dd / yyyy)

Promacta® (eltrombopag)
Hepatobiliary Laboratory Abnormalities

Section 1. Patient Information

Initials:	**PROMACTA *CARES* ID:**	**OCEANS Case No:** (For GSK use only)
Age:	**Date of Birth:** ____ / ____ / _____ (mm / dd / yyyy)	**Gender:** ☐ **Male** ☐ **Female**

Section 2. Promacta Therapy

Date when Promacta was started: ____ / ____ / _____ (mm / dd / yyyy)	**Is the patient still taking Promacta?** ☐ **Yes** ☐ **No**	**If YES, what was the dose of Promacta at the time of the event?** _____mg **If NO, what were the last dose and the date?** _____mg **Date:** ____ / ____ / _____ (mm / dd / yyyy)

Section 3. Adverse Event

What is the adverse event(s)?_____ **Date of this event:** ____ / ____ / _____ (mm / dd / yyyy)

Is this a serious adverse event? ☐ **Yes** ☐ **No**

If YES, please indicate the seriousness criteria below:

- ☐ **Death**
- ☐ **Hospitalization – initial or prolonged**
- ☐ **Congenital anomaly/birth defect**
- ☐ **Life-threatening**
- ☐ **Persistent or significant disability/incapacity**
- ☐ **Other,** (important medical events)_____

Outcome of the event:

- ☐ **Resolved**
- ☐ **Resolving/recovering**
- ☐ **Resolved with sequelae**
- ☐ **Not resolved**

Is this event related to treatment with Promacta? ☐ **Yes** ☐ **No**

Section 4. Current Liver Function Laboratory Tests

Please provide the following information regarding the current liver function laboratory tests for this event.

Dates (mm / dd / yyyy)	**Laboratory Test(s)**	**Reference range**
____ / ____ / _____	**Alanine Aminotransferase (ALT)** =	
____ / ____ / _____	**Aspartate Aminotransferase (AST)** =	
____ / ____ / _____	**Total Bilirubin** =	
____ / ____ / _____	**Direct Bilirubin** ***(only if total bilirubin is elevated)*** =	
____ / ____ / _____	**Alkaline Phosphatase** =	

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

Section 5. Liver Biopsy

Was a liver biopsy performed? ☐ **Yes** ☐ **No**

If YES, What were the results? _____

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

Section 6. Diagnostic Imaging

Were any of the following diagnostic imaging tests of the hepatobiliary system performed?

Yes	No	
☐	☐	**Liver Ultrasound**
☐	☐	**CAT Scan**
☐	☐	**MRI Scan**
☐	☐	**Endoscopic/Magnetic Retrograde Cholangiopancreatography (ERCP) / (MRCP)**
☐	☐	**Other_____**

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

Section 7. Medical Information

Does the patient have a history of drug allergies? ☐ **Yes** ☐ **No**

Any concomitant medication(s)? ☐ **Yes** ☐ **No** ☐ **None**

If YES, please list drug(s) below

Please list concurrent disease(s)

☐ **None**

Section 8. Liver Function Laboratory Tests - Peak and Return to Baseline Values

Please provide the following information regarding the peak and return to baseline liver function laboratory tests, if available.

Dates (mm / dd / yyyy)	**Laboratory Test(s)**	**Reference ranges**
_____ / ____ / _____ _____ / ____ / _____	**peak Alanine Aminotransferase (ALT) =** **return to baseline Alanine Aminotransferase =**	
_____ / ____ / _____ _____ / ____ / _____	**peak Aspartate Aminotransferase (AST) =** **return to baseline Aspartate Aminotransferase =**	
_____ / ____ / _____ _____ / ____ / _____	**peak total Bilirubin =** **return to baseline Bilirubin =**	
_____ / ____ / _____ _____ / ____ / _____	***(only if total bilirubin is elevated)*** **peak Direct Bilirubin =** **return to baseline Direct Bilirubin =**	
_____ / ____ / _____ _____ / ____ / _____	**peak Alkaline Phosphatase (Alk Phos) =** **return to baseline Alkaline Phosphatase =**	

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

Section 9. Reporter

☐ **PROMACTA *CARES* specialist** **Name and Title** _____

☐ **Healthcare Provider** **Name and Title** _____

☐ **Institution** **Name and Title** _____

☐ **Other (specify)** _____ **Name and Title** _____

smsg

Date of this report ____ / ____ / _____ **Signature**_____
(mm / dd / yyyy)

GlaxoSmithKline

Promacta® (eltrombopag)
Hematological Malignancy

Section 1. Patient Information

Initials:	**PROMACTA *CARES* ID:**	**OCEANS Case No:** (For GSK use only)
Age:	**Date of Birth:** ____ / ____ / _____ (mm / dd / yyyy)	**Gender:** ☐ **Male** ☐ **Female**

Section 2. Promacta Therapy

Date when Promacta was started: ____ / ____ / _____ (mm / dd / yyyy)	**Is the patient still taking Promacta?** ☐ **Yes** ☐ **No**	**If YES, what was the dose of Promacta at the time of the event?** _____mg **If NO, what were the last dose and the date?** _____mg **Date:** ____ / ____ / _____ (mm / dd / yyyy)

Section 3. Adverse Event

What is the adverse event(s)?_____ **Date of this event:** ____ / ____ / _____ (mm / dd / yyyy)

Is this a serious adverse event? ☐ **Yes** ☐ **No**

If YES, please indicate the seriousness criteria below:

- ☐ **Death**
- ☐ **Hospitalization – initial or prolonged**
- ☐ **Congenital anomaly/birth defect**
- ☐ **Life-threatening**
- ☐ **Persistent or significant disability/incapacity**
- ☐ **Other,** (important medical events)_____

Outcome of the event:

- ☐ **Resolved**
- ☐ **Resolving/recovering**
- ☐ **Resolved with sequelae**
- ☐ **Not resolved**

Is this event related to treatment with Promacta? ☐ **Yes** ☐ **No**

Section 4. Diagnosis

Please select one choice regarding this event:
☐ **New diagnosis** ☐ **Relapse of previous malignancy** ☐ **Unknown**

Please select one diagnosis from this list :

- ☐ **AML (FAB subtype):**_____
- ☐ **MDS (IPSS score):** _____
- ☐ **Lymphoma (specify):** _____
- ☐ **Under investigation**
- ☐ **Myeloproliferative Disease (MPD)**
  Please specify: ☐ **CML** ☐ **IMF** ☐ **PV** ☐ **ET**
- ☐ **Other,** (specify): _____

Is the peripheral blood smear abnormal? ☐ **Yes** ☐ **No**

Bone marrow aspirate? ☐ **Yes** ☐ **No**	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ **Yes** ☐ **No** **If YES, please specify:**
Bone marrow biopsy? ☐ **Yes** ☐ **No**	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ **Yes** ☐ **No** **If YES, please specify:**
Immunophenotype? ☐ **Yes** ☐ **No**	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ **Yes** ☐ **No** **If YES, please specify:**
Cytogenetics? ☐ **Yes** ☐ **No**	____ / ____ / _____ (mm / dd / yyyy)	**Abnormalities:** ☐ **Yes** ☐ **No** **If YES, please specify:**

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

Please provide any additional information on stage, treatment planned, pathology, and x-ray findings.

☐ **None**

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

What clinical features were present at the time of diagnosis? (check all that apply)

☐ **Anemia**
☐ **Pallor**
☐ **Fatigue**
☐ **Fever/night sweats**
☐ **Bone pain**
☐ **Hepatospenomegaly**
☐ **Granulocytopenia**
☐ **Thrombocytopenia**
☐ **Lymphadenopathy**
☐ **Increased bruising/bleeding**
☐ **Recurrent infection/poor wound healing**
☐ **Abdominal pain and /or weight loss**
☐ **Other** (please specify):_____

Section 5. Medical Information

Does the patient have any of the following past or present conditions that may predispose them to malignancies?

☐ **None**

Yes	No	
☐	☐	**Family History of malignancy**
☐	☐	**Smoking**
☐	☐	**Occupational exposure (e.g. benzene)**
☐	☐	**Monoclonal gammopathy**
☐	☐	**History of chemotherapy or radiation therapy**
☐	☐	**Other** (please specify)_____

What are the concomitant medications? (check all that apply)

☐ **None**
☐ **Azathioprine**
☐ **Corticosteroids**
☐ **Cyclophosphamide**
☐ **Danazol**
☐ **Interferon alpha**
☐ **IVIg**
☐ **Rituximab**
☐ **Other** (please specify):_____

Section 6. Reporter

☐ **PROMACTA *CARES* specialist** **Name and Title** _____
☐ **Healthcare Provider** **Name and Title** _____
☐ **Institution** **Name and Title** _____
☐ **Other (specify)** _____ **Name and Title** _____

smsg

Date of this report ____ / ____ / _____ **Signature**_____
(mm / dd / yyyy)

GlaxoSmithKline

Promacta® (eltrombopag)
Worsening Thrombocytopenia and Bleeding

Section 1. Patient Information

Initials:	**PROMACTA *CARES* ID:**	**OCEANS Case No:** (For GSK use only)
Age:	**Date of Birth:** ____ / ____ / _____ (mm / dd / yyyy)	**Gender:** ☐ Male ☐ Female

Section 2. Promacta Therapy

Date when Promacta was started: ____ / ____ / _____ (mm / dd / yyyy)	**Is the patient still taking Promacta?** ☐ Yes ☐ No	**If YES, what was the dose of Promacta at the time of the event?** _____mg **If NO, what were the last dose and the date?** _____mg **Date:** ____ / ____ / _____ (mm / dd / yyyy)

Section 3. Adverse Event

What is the adverse event(s)?_____ **Date of this event:** ____ / ____ / _____ (mm / dd / yyyy)

Is this a serious adverse event? ☐ Yes ☐ No

If YES, please indicate the seriousness criteria below:

- ☐ **Death**
- ☐ **Hospitalization – initial or prolonged**
- ☐ **Congenital anomaly/birth defect**
- ☐ **Life-threatening**
- ☐ **Persistent or significant disability/incapacity**
- ☐ **Other,** (important medical events)_____

Outcome of the event:

- ☐ **Resolved**
- ☐ **Resolving/recovering**
- ☐ **Resolved with sequelae**
- ☐ **Not resolved**

Is this event related to treatment with Promacta? ☐ Yes ☐ No

What is the platelet count most proximal to this event? _____unit_____ **Normal range**_____

Describe any bleeding symptoms during the event? ☐ None

Was a transfusion required to maintain the baseline hemoglobin? ☐ Yes ☐ No **If yes, how many?** _____

Please provide the date(s)

Please provide up to the last four platelet counts <u>before</u> the first day of treatment with Promacta.

☐ **Date** _____ **Platelet count** _____ **Normal range**_____

☐ **Date** _____ **Platelet count** _____ **Normal range**_____

☐ **Date** _____ **Platelet count** _____ **Normal range**_____

☐ **Date** _____ **Platelet count** _____ **Normal range**_____

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

Section 4. Medical Information

Were there any similar bleeding events prior to therapy with Promacta? ☐ **Yes** ☐ **No**
If YES, please describe:

Has the patient experienced bleeding symptoms on discontinuation of <u>other treatments</u> for ITP? ☐ **Yes** ☐ **No**
If YES, please describe:

Please list concurrent disease(s) ☐ **None**

Were there any changes to the concomitant therapy(ies) for ITP prior to this event? ☐ **Yes** ☐ **No**
If YES, please specify:

Please list concurrent medication(s) (e.g. anti-platelet medications, NSAIDs) ☐ **None**

Section 5. Reporter

☐ **PROMACTA *CARES* specialist** **Name and Title** _____
☐ **Healthcare Provider** **Name and Title** _____
☐ **Institution** **Name and Title** _____
☐ **Other (specify)** _____ **Name and Title** _____

smsg

Date of this report ____ / ____ / _____ **Signature**_____
(mm / dd / yyyy)

Promacta® (eltrombopag)
Thrombotic and Thromboembolic Events

Section 1. Patient Information

Initials:	**PROMACTA *CARES* ID:**	**OCEANS Case No:** (For GSK use only)
Age:	**Date of Birth:** ____ / ____ / _____ (mm / dd / yyyy)	**Gender:** ☐ Male ☐ Female

Section 2. Promacta Therapy

Date when Promacta was started: ____ / ____ / _____ (mm / dd / yyyy)	**Is the patient still taking Promacta?** ☐ Yes ☐ No	**If YES, what was the dose of Promacta at the time of the event?** _____mg **If NO, what were the last dose and the date?** _____mg **Date:** ____ / ____ / _____ (mm / dd / yyyy)

Section 3. Adverse Event

Adverse Event(s)_____ **Date of this event:** ____ / ____ / _____ (mm / dd / yyyy)

What was the <u>most proximal</u> platelet count to the time of this event? **Date:** ____ / ____ / _____ (mm / dd / yyyy)

What was the platelet count <u>after</u> this event? **Date:** ____ / ____ / _____ (mm / dd / yyyy)

Is this a serious adverse event? ☐ Yes ☐ No

If YES, please indicate the seriousness criteria below:

- ☐ **Death**
- ☐ **Hospitalization – initial or prolonged**
- ☐ **Congenital anomaly/birth defect**
- ☐ **Life-threatening**
- ☐ **Persistent or significant disability/incapacity**
- ☐ **Other,** (important medical events)_____

Outcome of the event:

- ☐ **Resolved**
- ☐ **Resolving/recovering**
- ☐ **Resolved with sequelae**
- ☐ **Not resolved**

Is this event related to treatment with Promacta? ☐ Yes ☐ No

Section 4. Diagnostic Tests

Yes	No	
☐	☐	**CT Scan**
☐	☐	**Phlebography**
☐	☐	**Doppler/Ultrasound**
☐	☐	**V/P scintigraphy**
☐	☐	**Echocardiography**
☐	☐	**ECG**
☐	☐	**Blood-gas analysis**

Other tests? **Please specify** _____
_____

Please provide anonymized copy of these reports, if available.
☐ **Check this box, if attached**

Thrombophilic Laboratory Profile

Normal	Abnormal	Not Done	
☐	☐	☐	**Lupus anticoagulants**
☐	☐	☐	**Antiphospholipid antibodies**
☐	☐	☐	**Anti-prothombin antibodies**
☐	☐	☐	**Beta 2 glycoprotein antibodies**
☐	☐	☐	**Factor VIII**
☐	☐	☐	**Protein C**
☐	☐	☐	**Protein S**
☐	☐	☐	**Serum homocysteine**
☐	☐	☐	**Anti-thrombin III**

Thrombophilic Laboratory Profile continued

Normal	Abnormal	Not Done				
☐	☐	☐	**Factor V Leiden mutation**	☐Heterozygous	☐Homozygous	☐Unknown
☐	☐	☐	**Prothrombin mutation**	☐Heterozygous	☐Homozygous	☐Unknown
☐	☐	☐	**MTHFR-Polymorphism**	☐Heterozygous	☐Homozygous	☐Unknown

You may attach anonymized copy of these reports, if available. ☐ **Check this box, if attached**

Section 5. Medical Information

Please indicate below if the patient has ever had any of the following conditions.

☐ **None**

Yes	No	
☐	☐	**Hypertension**
☐	☐	**Diabetes Mellitus**
☐	☐	**Hyperlipidemia**
☐	☐	**Cardiovascular disease**
☐	☐	**Thromboembolic event**
☐	☐	**Family history of thromboembolism**
☐	☐	**Varicose Vein(s)**

RISK FACTORS

Yes	No	
☐	☐	**Was there trauma prior to the event?**
☐	☐	**Was the patient immobilized /hospitalized prior to this event (e.g. surgical procedures)?**
		If YES, was prophylactic anticoagulation administered? ☐**Yes** ☐**No**
☐	☐	**If female, is the patient taking oral contraceptives?**
☐	☐	**If female, has the patient taken hormone replacement therapy?**
☐	☐	**Evidence of any autoimmune disease at any time other than ITP (e.g. IBD, SLE, RhA, etc.)?**
		If YES, please describe:

Please list past or concomitant medication(s) (e.g. IVIG, diuretics, corticosteroids, aminocaproic acid, antifibrinolytic agents, etc.)

☐ **None**

Section 6. Reporter

☐ **PROMACTA *CARES* specialist** **Name and Title** _____

☐ **Healthcare Provider** **Name and Title** _____

☐ **Institution** **Name and Title** _____

☐ **Other (specify)** _____ **Name and Title** _____

Date of this report ____ / ____ / _____ **Signature**_____

(mm / dd / yyyy)

Survey Instrument to Assess the Risk Management Plan Education for HCPs

Objective

To assess the effectiveness of the communication of the key PROMACTA REMS Messages to enrolled MDs.

Overview

Sponsor commits to assessing the effectiveness of the REMS's educational efforts through unbiased surveys of a representative sample of enrolled MDs responsible for prescribing PROMACTA. The surveys will be conducted by an experienced, independent third-party market research provider, National Analysts Worldwide. All enrolled MDs will be invited to participate in each of two surveys administered at 12 and 18 months post-launch. The goal is to achieve an overall accuracy level of 80% on pre-selected questions related to REMS messages. Accuracy will be calculated by dividing the number of correct responses by the total number of questions, but diagnostics will be available through calculation of accuracy on every question.

The survey may contain questions not related to the Key REMS Messages. Only those questions directly related to the Key REMS Messages will be used to calculate the response rate. Sponsor will continue surveys at 12 month intervals thereafter should the 80% target rate not be achieved.

Detailed Study Design & Methodology

The Sponsor has submitted Study Design and Methodology for surveying enrolled MDs to evaluate the success of the education program for the Product. It is anticipated that all the physicians who enroll will be hematologists or hematologist/oncologists.

- **Sample Design**

  Respondents will be recruited from the list of physicians who have enrolled to prescribe PROMACTA and agreed to be contacted for market research purposes. Recruiting will occur via phone, fax or e-mail.

  Sample size per wave will be determined by the number of MDs who enroll to

prescribe PROMACTA. The current sampling projections assume that there are 2,500 MDs in the target list and 50% or 1,250 MDs enroll within the first twelve months after PROMACTA becomes available, and that another 1,250 MDs enroll between months twelve and eighteen. The Sponsor is proposing to sample 100 MDs in Wave 1 and 100 MDs in Wave 2, assuming an 8% response rate, which represents a typical yield from survey research*. Respondents from Wave 1 will not be eligible in Wave 2.

* The ability to meet the aforementioned sample sizes is dependant upon assumptions, including but not limited to, the number of enrolled physicians, and overall response rate for participation. It is important to note that a reevaluation of sample size might be required if these assumptions fall short.

- **Data Collection**

  Surveys will be conducted via the internet, an approach that has nearly supplanted all forms of survey data collection (at least among healthcare professionals) in the last decade. Notably, the high rate of internet penetration among healthcare professionals makes it extremely efficient and there is less concern about recording error when respondents are typing responses rather than interviewers. If desired, the survey can also be made available via telephone, but it is rare to find a healthcare professional who will take a survey by phone but not by web.

- **Survey Scope**

  All potential respondents will be invited to visit the National Analysts Worldwide website to take a survey on the treatment of ITP. The sponsor(s) of the study will, of course, not be disclosed.

  The study design for the survey will be comprised of:

  - A single screener question to ensure that respondents are aware that they have enrolled to prescribe PROMACTA

  - Questions designed to assess knowledge of Key REMS Messages, including: (a) indication; (b) known risks; (c) understanding of the program.

- Upon conclusion of the survey, a reinforcement of the REMS information will be provided to participants who answered the questions correctly and a redirection will be provided to physicians who answered incorrectly. In this manner, the survey itself can be used as a means of education reinforcement for the Key REMS messages.

- **Survey Pretest**

  Prior to the first wave of the research, the third-party market research vendor will conduct approximately four pre-tests. In this pretest, enrolled physicians will complete the survey and then be de-briefed by a trained moderator. The pretest will serve to hone the questions to be utilized in the quantitative study, and to ensure that none of the questions induce bias. The Sponsor will submit the data collected via these survey pretests along with results from the corresponding wave of research.

Confidence Intervals for Projected Sample Sizes

The recommended sample sizes establish confidence intervals of 8 percentage points in Wave 1 and 6 percentage points in Wave 2 at the 95% confidence level if 80% of the questions are answered correctly.

TABLE OF CONFIDENCE INTERVALS BY SAMPLE SIZE AND % CORRECT

- Alpha = .05 -

	PERCENT CORRECT								
Sample Size	**10%**	**20%**	**30%**	**40%**	**50%**	**60%**	**70%**	**80%**	**90%**
50	8%	11%	13%	14%	14%	14%	13%	11%	8%
100	6%	8%	9%	10%	10%	10%	9%	8%	6%
150	5%	6%	7%	8%	8%	8%	7%	6%	5%
200	5%	6%	6%	7%	7%	7%	6%	6%	5%

Survey Controls for Bias

Administration Bias

To minimize bias, the Sponsor will engage a third-party market research provider (Surveyor) to conduct the surveys

Sampling Bias

A random sample will be selected for each wave among the enrolled physicians prior to each wave to minimize sampling bias. Surveyor will be instructed to randomly sample the participants in the list, which is expected to engage an appropriate cross-section of HCPs. Once surveyed, respondents will be removed from the physician database and will not be eligible to participate in future waves of this study. The screening question will be designed to encourage participation by all levels of the product users. Also, multiple attempts will be made to recruit respondents from the sample, thus minimizing non-response bias.

Questionnaire Bias

Surveyor will ensure that survey bias is minimized through the application of careful research methods, including but not limited to, randomization of response lists within questions, carefully constructed non-leading questions, and a pretest which will serve to ensure the clarity of the questions.

SURVEY

- **Screen for Enrolled MDs**
- **Respondents will be prevented from altering their previous responses.**
- **Questions shaded in GREEN indicate pre-selected questions to evaluate awareness of the key REMS messages (involved in calculation of accuracy rate).**

Screener

S1. Have you enrolled to prescribe PROMACTA?

o Yes **INVITE TO PARTICIPATE**

o No **TERMINATE**

---

1. What is your medical field of specialty? Select one.

Hematologist
Hematologist/Oncologist
Other (Specify_____)

2. For what condition is PROMACTA indicated? Select one.

ITP	o
Hemophilia	o
Leukemia	o
Other (Specify _____)	o
Don't know/Not Sure	o

[PROGRAMMER: RANDOMIZE THE ORDER OF THE FIRST THREE ROWS]

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3. According to the prescribing information, which of the following are risks associated with PROMACTA? Select all that apply.

Hepatoxicity/Hepatic effects	☐
Bone Marrow Reticulin and Risk for Bone Marrow Fibrosis	☐
Worsened Thrombocytopenia after Cessation of PROMACTA	☐
Thrombotic/thromboembolic Complications	☐
Malignancies and Progression of Malignancies	☐
Anaphalaxis	☐
Stevens-Johnson Syndrome	☐

4. After establishing a stable dose of PROMACTA, how often is it necessary to monitor a patient's CBCs, including platelet counts and peripheral blood smears?

Weekly	
Every two weeks	
Monthly	
Every two months	

5. During the dose adjustment phase for PROMACTA, how often is it necessary to monitor serum liver tests (ALT, AST, bilirubin) in a patient?

Weekly	
Every two weeks	
Monthly	
Every two months	

6. How long after initiating PROMACTA do you need to reauthorize a patient to continue on PROMACTA?

One month	
Three months	
Six months	
One year	

7. It is necessary to complete the PROMACTA *CARES* Patient Discontinuation and Post-Therapy Follow-up Form at the time of discontinuation of PROMACTA and three months later.

True	
False	

[PROGRAMMER: RANDOMIZE THE ORDER OF THE ROWS]

8. Physicians cannot prescribe PROMACTA unless they have enrolled in restricted distribution program (i.e., PROMACTA *CARES)*.

True	
False	

9. Patients cannot receive PROMACTA unless they have enrolled in a restricted distribution program (i.e., PROMACTA CARES).

True	
False	

SHOW TO PHYSICIANS WHO ANSWERED Q1 OR Q2 INCORRECTLY

Thank you for participating in this study. Please note that you answered incorrectly to the following question(s). The correct information regarding appropriate use of PROMACTA as presented in the product labeling is as follows. Please be mindful of this information when using this medication:

INSERT QUESTION(S) HIGHLIGHTING CORRECTED RESPONSE

SHOW TO PHYSICIANS WHO ANSWERED Q1 and Q2 CORRECTLY

Thank you for participating in this study. Please note that you answered correctly to the following questions regarding appropriate use of PROMACTA as presented in the product labeling. Please continue to be mindful of this information.

INSERT QUESTION(S) HIGHLIGHTING CORRECT RESPONSE

PROMACTA *CARES* Compliance Monitoring

PROMACTA *CARES* will measure and assess adherence to the program requirements on an on-going basis.

Prescriber Compliance

PROMACTA *CARES* will evaluate prescriber compliance on a monthly basis by an assessment of completion of the Patient Baseline Form, Medical and Reauthorization Form, complying with the Discontinuation Procedure, and Post-Discontinuation Follow-Up Procedures for each patient.

Controlled Distribution Compliance

A shipment authorization code will be provided from GSK with each shipment of PROMACTA. The authorization code is a unique code that will provide a traceable number for each shipment, and it is only provided after confirmation that the Health Care Provider is authorized to receive PROMACTA.

On a monthly basis, the single distributor (GSK) will provide shipment authorization codes as well as other information critical to monitoring shipments to authorized pharmacies and inventory levels and will reconcile the shipping addresses that have received PROMACTA shipments against the list of authorized pharmacies.

Using information contained in the PROMACTA *CARES* database, specific items to reconcile include: shipment authorization code as obtained from PROMACTA *CARES* database for each shipment and the amount of drug shipped to each site compared to the actual patient treatment prescriptions/orders for enrolled patients at the authorized pharmacy. These reconciliations will be conducted by a third-party by analyzing beginning inventory balances (including bulk and prescription fill quantities), product shipped in/out during the reconciliation period, product returns, and the number of confirmed patient prescription/orders dispensed by the authorized pharmacy. Any discrepancies identified by this reconciliation would be flagged for further investigation by GSK.

Such reconciliation noting discrepancies could require additional for-cause audits of physical inventory at the authorized pharmacy on an as-needed basis.

Pharmacy Compliance

Measurement of enrolled pharmacy (specialty pharmacies, hospital pharmacies (in-patient and out-patient), and physician dispensing clinics) adherence to the REMS will be completed on a monthly basis by review of the Inventory Tracking Log; the pharmacy will be required to fax the Inventory Tracking Log monthly to PROMACTA *CARES.*

Review of the Inventory Tracking Log allows the following:

- An assessment of the amount of drug shipped to each site compared to the actual patient orders by cross match of dispensing data provided by the enrolled pharmacy and GSK distribution data residing in the PROMACTA *CARES* databases.

- An assessment of pharmacy compliance with documentation of the unique prescription verification number for each PROMACTA prescription/refill. This verification is unique to the patient (PID#) and the prescription/refill. The pharmacy will document this unique prescription verification number in the Pharmacy Inventory Tracking Log. This unique prescription verification number allows the measurement of pharmacy adherence to the REMS by confirming all prescriptions dispensed have an associated unique prescription verification number documented.

Non-Compliance

Prescribers

PROMACTA *CARES* will contact identified non-compliant prescribers via telephone or letter to emphasize the program requirements and the importance of compliance with the program. If a prescriber remains non-compliant, PROMACTA *CARES* will contact the prescriber again via telephone and/or letter and a GSK account manager will provide additional educational or training support to the prescriber. If a prescriber continues to be repeatedly non-compliant GSK may take additional action up to and including revoking the prescriber's ability to enroll or prescribe PROMACTA to new patients, until re-training by GSK takes place. The prescriber will still be able to prescribe PROMACTA to existing patients.

If a prescriber continues to be repeatedly non-compliant after GSK has made attempts to resolve the non-compliance (verbal and written contact, additional training, etc.), GSK may take additional action up to and including suspending the prescriber's ability to prescribe PROMACTA with PROMACTA *CARES*. GSK will evaluate these situations on a case-by-case basis and make every attempt to work with the prescriber on re-training efforts to keep their enrolment status active as to avoid the impact to the patient's access to PROMACTA.

Pharmacy

GSK will attempt to retrain a non-compliant pharmacy. The pharmacy will be de-authorized if non-compliance persists after re-training until the pharmacy can demonstrate sufficient controls and procedures to prevent re-occurrence of non-compliance. Patients with active PROMACTA prescriptions from a de-authorized pharmacy will be transferred to another authorized pharmacy of their choice.

GlaxoSmithKline

NDA 22291 PROMACTA® (eltrombopag)

Falsification of forms and/or data submissions by either prescribers or pharmacies will result in additional corrective action up to and including de-enrollment.