RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Promacta is used to treat patients with chronic immune thrombocytopenia (ITP), who have not responded adequately to corticosteroids, immunoglobulins, or to the removal of their spleen (splenectomy). ITP is a blood disorder that results in a low number of platelets which can lead to serious bleeding. Promacta works by stimulating the bone marrow to produce needed platelets (1).

Regulatory Status
FDA-approved indication: Promacta is a thrombopoietin receptor agonist indicated for the treatment of:

1. Thrombocytopenia in adult and pediatric patients 1 year and older with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
2. Thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy
3. Patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy
4. In combination with standard immunosuppressive therapy for first line treatment of adult and pediatric patients 2 years and older with severe aplastic anemia

Limitations of Use: (1)

1. Promacta should not be used to normalize platelet counts.
2. Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
3. Promacta should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon therapy or limits the ability to maintain optimal interferon-based therapy.
4. Safety and efficacy have not been established in combination with direct acting antiviral agents approved for treatment of chronic hepatitis C infection.

Promacta carries a boxed warning regarding the risk for hepatotoxicity. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels must be measured prior to initiation of Promacta, every 2 weeks during the dose adjustment phase, and monthly.

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following establishment of a stable dose. Monitor serum liver tests weekly until the abnormality(ies) resolve, stabilize, or return to baseline levels. Promacta should be discontinued for the development of important liver test abnormalities. Promacta, in combination with interferon and ribavirin in patients with chronic hepatitis C, may increase the risk of hepatic decompensation (1).

Promacta must be discontinued if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks of therapy at the maximum daily dose of 75mg. Discontinue Promacta if ALT levels increase to ≥3X upper limit of normal (ULN) in patients with normal liver function or ≥3X baseline in patients with pre-treatment elevations in transaminases and are: 1) progressive 2) persistent for ≥4 weeks 3) accompanied by increased direct bilirubin, or 4) accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation. Promacta should be discontinued when antiviral therapy is discontinued (1).

Promacta must be held when platelet levels reach >400 x 10⁹/L and platelet levels monitored twice weekly to evaluate any decrease in levels and need for re-initiation of therapy. If platelet levels remain above 400 x 10⁹/L after two weeks, Promacta therapy must be discontinued. If platelet count drops to <150 x 10⁹/L, therapy can be restarted at a decreased dose (1).

Thrombotic/thromboembolic complications may result from increases in platelet counts with Promacta. There is an increased risk of thromboembolism when administering Promacta to patients with known risk factors (e.g., Factor V Leiden, ATIII deficiency, antiphospholipid syndrome, chronic liver disease). To minimize the risk for thrombotic/thromboembolic complications, do not use Promacta in an attempt to normalize platelet counts (1).

During the dose adjustment phase of therapy, complete blood counts (CBCs) with differentials (including platelet counts) should be obtained weekly then monthly after stabilization of dose, then weekly for 4 weeks after discontinuation of therapy (1).

The safety and efficacy of Promacta in pediatric patients 1 year of age and younger with chronic ITP have not been established. The safety and efficacy of Promacta in patients 2 years of age and younger with severe aplastic anemia has not been established. The safety and efficacy of Promacta in pediatric patients with thrombocytopenia associated with chronic hepatitis C have not been established (1).
Summary

Promacta is indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy and their platelet count at the time of diagnosis was less than $50 \times 10^9/L$. Promacta is also indicated for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy and their platelet count at time of diagnosis was less than $75 \times 10^9/L$. Promacta is also indicated for the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy and their platelet count at the time of diagnosis was less than $50 \times 10^9/L$, or as first line therapy in patients 2 years and older in combination with standard immunosuppressive therapy. The safety and efficacy of Promacta in pediatric patients 1 year of age and younger with chronic ITP have not been established. The safety and efficacy of Promacta in patients 2 years of age and younger with severe aplastic anemia has not been established. The safety and efficacy of Promacta in pediatric patients with thrombocytopenia associated with chronic hepatitis C have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Promacta while maintaining optimal therapeutic outcomes.

References