VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

PROMACTA™ (eltrombopag)

Effective Date: 10/23/12
Date Developed: 10/15/12 by Albert Reeves MD
Last Approval Date: 1/26/16, 1/24/17, 1/23/18

(Archived 1/22/19)

PROMACTA™ is Colony Stimulating Factor; Thrombopoietic Agent. It is used for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) at risk for bleeding who have had insufficient response to corticosteroids, immune globulin, or splenectomy.

Pre-Authorization Criteria:

VCHCP will authorize Promacta for FDA indicated treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) at risk for bleeding who have had insufficient response to corticosteroids, immune globulin, or splenectomy.

VCHCP requires that Promacta be prescribed by Hematologist.

DOSAGE FORMS AND STRENGTHS

Tablet, oral: Promacta®: 25 mg, 50 mg, 75 mg

Dosing: Adult

Use the lowest dose to achieve and maintain platelet count ≥50,000/mm^3 as needed to reduce the risk of bleeding. Adjust dose based on platelet count response; initial platelet response generally occurs within 1-2 weeks. Discontinue if platelet count does not respond to a level that avoids clinically important bleeding after 4 weeks at the maximum daily dose of 75 mg.

Immune (idiopathic) thrombocytopenic purpura (ITP): Oral: Initial: 50 mg once daily; adjust dose to achieve and maintain platelet count ≥50,000/mm^3 to reduce the risk of bleeding; maximum dose: 75 mg once daily.

Initial dosage for patients of East-Asian ethnicity (eg, Chinese, Japanese, Korean, Taiwanese): Oral: 25 mg once daily

Dosage adjustment recommendations (based on platelet response):

Platelet count <50,000/mm^3 (after at least 2 weeks): Increase daily dose by 25 mg (if taking 12.5 mg once daily, increase dose to 25 mg once daily prior to increasing the dose amount by 25 mg/day); maximum dose: 75 mg/day

Platelet count ≥200,000/mm^3 and ≤400,000/mm^3 (at any time): Reduce daily dose by 25 mg; reassess in 2 weeks

Platelet count >400,000/mm^3 : Withhold dose; assess platelet count twice weekly; when platelet count <150,000/mm^3, resume with the daily dose reduced by 25 mg (if taking 25 mg once daily, resume with 12.5 mg once daily)

Platelet count >400,000/mm^3 after 2 weeks at the lowest dose: Discontinue treatment

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow reticulin: May increase the risk for bone marrow reticulin formation or progression; collagen fibrosis (not associated with cytopenias) was observed in clinical trials. In an extension study, myelofibrosis (≤grade 1) was observed in a majority of bone marrow biopsies performed after 1 year of treatment. Risk of bone marrow fibrosis with clinical ramifications has not been excluded in clinical trials. Monitor peripheral blood smear for cellular morphologic abnormalities; analyze CBC monthly; discontinue treatment with onset of new or worsening abnormalities (eg, teardrop and nucleated RBC, immature WBC) or cytopenias and consider bone marrow biopsy (with staining for fibrosis).

• Cataract formation: Cataract formation or worsening was observed in clinical trials. Monitor regularly for signs and symptoms of cataracts; obtain ophthalmic exam at baseline and during therapy. Use with caution in patients at risk for cataracts (eg, advanced age, long-term glucocorticoid use).

• Hepatotoxicity: **[U.S. Boxed Warning]: May cause hepatotoxicity; obtain ALT, AST, and bilirubin prior to treatment initiation, every 2 weeks during adjustment phase, then monthly (after stable dose established). Obtain fractionation for elevated bilirubin levels. Repeat abnormal liver function tests within 3-5 days; if confirmed abnormal, monitor weekly until resolves, stabilizes, or returns to baseline. Discontinue treatment for ALT levels ≥3 times the upper limit of normal (ULN) and which are progressive, or persistent (≥4 weeks), or accompanied by increased direct bilirubin, or accompanied by clinical signs of liver injury or evidence of hepatic decompensation**. Reinitiation is not recommended; hepatotoxicity usually

recurred with retreatment after therapy interruption; however, if the benefit of treatment outweighs the hepatotoxicity risk, initiate carefully, and monitor liver function tests weekly during the dose adjustment phase. Permanently discontinue if hepatotoxicity recurs with rechallenge.

• Malignancy/tumorigenicity: Stimulation of cell surface thrombopoietin (TPO) receptors may increase the risk for hematologic malignancies.

• Thromboembolism: Thromboembolism (venous or arterial) may occur with excess increases in platelet levels. Use with caution in patients with known risk factors for thromboembolism (eg, Factor V Leiden, ATIII deficiency, antiphospholipid syndrome, chronic liver disease). Portal venous thrombosis was reported in a study of non-ITP patients with chronic liver disease (not an FDA-approved indication) receiving eltrombopag 75 mg once daily for 14 days as a preparative regimen prior to invasive procedures to reduce platelet transfusions.

REFERENCES

1. Bussel JB, Cheng G, Saleh MN, et al, "Eltrombopag for the Treatment of Chronic Idiopathic Thrombocytopenic Purpura," *N Engl J Med*, 2007, 357(22):2237-47. [PubMed 18046028]

2. Bussel JB, Provan D, Shamsi T, et al, "Effect of Eltrombopag on Platelet Counts and Bleeding During Treatment of Chronic Idiopathic Thrombocytopenic Purpura: A Randomised, Double-Blind, Placebo-Controlled Trial," *Lancet*, 2009, 373(9664):641-8. [PubMed 19231632]

3. Cheng G, Saleh MN, Marcher C, et al, "Eltrombopag for Management of Chronic Immune Thrombocytopenia (RAISE): A 6-Month, Randomised, Phase 3 Study," *Lancet*, 2011, 377(9763):393-402. [PubMed 20739054]

4. Jenkins JM, Williams D, Deng Y, et al, "Phase 1 Clinical Study of Eltrombopag, An Oral, Nonpeptide Thrombopoietin Receptor Agonist," *Blood*, 2007, 109(11):4739-41. [PubMed 17327409]

5. Kuter DJ, "New Thrombopoietic Growth Factors," *Blood*, 2007, 109(11):4607-16. [PubMed 17289815]

6. Matthys G, Park JW, McGuire S, et al, "Eltrombopag Does Not Affect Cardiac Repolarization: Results From a Definitive QTc Study in Healthy Subjects," *Br J Clin Pharmacol*, 2010, 70(1):24-33. [PubMed 20642544]

7. McHutchison JG, Dusheiko G, Schiffman ML, et al, "Eltrombopag for Thrombocytopenia in Patients With Cirrhosis Associated With Hepatitis C," *N Engl J Med*, 2007, 357(22):2227-36. [PubMed 18046027]

8. Pecci A, Gresele P, Klersy C, et al, "Eltrombopag for the Treatment of the Inherited Thrombocytopenia Deriving From MYH9 Mutations," *Blood*, 2010, 116(26):5832-7. [PubMed 20844233]

9. Williams DD, Peng B, Bailey CK, Effects of Food and Antacids on the Pharmacokinetics of Eltrombopag in Healthy Adult Subjects: Two Single-Dose, Open-Label, Randomized-Sequence, Crossover Studies," *Clin Ther*, 2009, 31(4):764-76. [PubMed 19446149]

10. ©2013 UpToDate® - www.uptodate.com

Revision History:

Date Reviewed/No Updates: 1/16/13
Date Approved by P&T Committee: 10/23/12; 1/29/13
Date Reviewed/No Updates: 1/28/14 by C. Sanders MD
Date Approved by P&T Committee: 1/28/14
Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD
Date Approved by P&T Committee: 1/27/15
Date Reviewed/No Updates: 1/26/16 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/26/16
Date Reviewed/No Updates: 1/24/17 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/24/17
Date Reviewed/No Updates: 1/23/18 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/23/18
Date Reviewed/Archived: 1/22/19 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/22/19

Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Archived – check ESI