VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Thrombocytopenia – Promacta® (eltrombopag tablets and oral suspension – Novartis)

TAC APPROVAL DATE: 07/03/2019

OVERVIEW

Promacta is also indicated for the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy. Also, Promacta is indicated for use in combination with standard immunosuppressive therapy for the first-line treatment of adult and pediatric patients ≥ 2 years of age with severe aplastic anemia. Promacta, a thrombopoietin receptor agonist, has several indications.[1] It is indicated for the treatment of thrombocytopenia in adult and pediatric patients ≥ 1 year of age with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.[1] Promacta is also indicated for the treatment of thrombocytopenia in patients with chronic hepatitis C (CHC) to allow initiation and maintenance of interferon-based therapy. Use Promacta only in patients with CHC whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy. The safety and efficacy of Promacta have not been established in combination with direct-acting antiviral agents used without interferon for the treatment of chronic hepatitis C infection.

Guidelines

Aplastic Anemia

Guidelines for the diagnosis and management of adult aplastic anemia are also available for the British Society.[2] The current standard first-line immunosuppressive therapy is horse ATG (ATG-ATGAM) combined with cyclosporine. Immunosuppressive therapy is recommended first-line for non-severe aplastic anemia in patients requiring treatment, severe or very severe aplastic anemia in patients who lack a matched sibling donor, and severe or very severe aplastic anemia in patients > 35 to 50 years. Other immunosuppressive recommended have been studied (e.g., mycophenolate mofetil, sirolimus, corticosteroids) but expertise should be provided prior to consideration of such agents. Hematopoietic stem cell transplantation (HSCT) is also recommended in certain circumstances. Promacta is an option is some clinical scenarios (e.g., heavily pre-treated patients, those unsuitable for HSCT).

ITP

In 2011 the American Society of Hematology published an evidence-based practice guideline for immune thrombocytopenia.[3] First-line treatment for adults includes corticosteroids or intravenous immunoglobulin (IVIG). For patients who are unresponsive or relapse after initial corticosteroid therapy splenectomy is recommended. Thrombopoietin receptor agonists are recommended for patients with a bleeding risk who relapse following splenectomy, or have a contraindication to splenectomy and who have failed at least one other therapy. The guidelines also suggest that thrombopoietin receptor agonists be considered for those at risk of bleeding who have failed one line of therapy, such as corticosteroids or IVIG, and who have not undergone splenectomy. Rituximab is recommended in certain patients who have not responded to other therapies. Regarding children, the guidelines state that studies of thrombopoetin receptor agonists in children and adolescents have been initiated.

Myelodysplastic Syndrome (MDS)
Current recommendations from the National Comprehensive Cancer Network (NCCN) for MDS (version 2.2019 – October 18, 2018) state to consider treatment with a thrombopoietin receptor agonist in patients with lower-risk MDS who have severe or life-threatening thrombocytopenia.[4] The data with Promacta are discussed noting increased rate of platelet response and decreased overall bleeding events among patients with low to intermediate risk MDS. Of note, data are available that describe the use of Promacta in patients with MDS.[5-7]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Promacta. Because of the specialized skills required for evaluation and diagnosis of patients treated with Promacta as well as the monitoring required for adverse events and efficacy, approval requires Promacta to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Promacta is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Aplastic Anemia.** Approve for 1 year if the patient meets the following criteria (A, B and C):
   - **A)** The patient has low platelet counts at baseline (pretreatment) [e.g., < 30 x 10^9/L {< 30,000/µL}]; AND
   - **B)** Promacta is prescribed by, or in consultation with, a hematologist; AND
   - **C)** The patient meets one of the following (i or ii):
     - **i.** The patient had tried at least one immunosuppressant therapy. Note: Examples of therapies are cyclosporine, Atgam® (lymphocyte immune globulin, anti-thymocyte globulin [equine] sterile solution for intravenous use only), mycophenolate moefetil, or sirolimus; OR
     - **ii.** The patient will be using Promacta in combination with standard immunosuppressive therapy. Note: Examples of therapies are cyclosporine, Atgam® (lymphocyte immune globulin, anti-thymocyte globulin [equine] sterile solution for intravenous use only), mycophenolate moefetil, or sirolimus.

2. **Chronic Immune Thrombocytopenia.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** The agent is prescribed by, or in consultation with, a hematologist; AND
   - **B)** The patient meets ONE of the following criteria (i or ii):
     - **i.** The patient has tried at least one other therapy. Note: Examples of therapies are corticosteroids, intravenous immunoglobulin, anti-D immunoglobulin, Nplate® (romiplostim injection for subcutaneous use), Tavalisse™ (fostamatinib disodium hexahydrate tablets), Doptelet® (avatrombopag tablets), or rituximab; OR
     - **ii.** The patient has undergone splenectomy.

3. **Treatment of Thrombocytopenia in Patients with Chronic Hepatitis C.** Approve for 1 year if the patient meets the following criteria (A, B, and C):

A) Promacta is prescribed by, or in consultation with, either a gastroenterologist, a hepatologist, or a physician that specializes in infectious disease; AND
B) The patient has low platelet counts at baseline (pretreatment) [e.g., < 75 x 10^9/L {< 75,000/µL}]; AND
C) The patient will be receiving interferon-based therapy for chronic hepatitis C. Note: Examples of therapies are pegylated interferon (Pegasys® [peginterferon alfa-2a injection], PegIntron® [peginterferon alfa-2b injection], or Intron A® (interferon alfa-2b).

Other Uses with Supportive Evidence

4. Thrombocytopenia in Myelodysplastic Syndrome (MDS). Approve Promacta for 1 year if the patient meets the following criteria (A, B and C):
A) The agent is prescribed by, or in consultation with, a hematologist or an oncologist; AND
B) The patient has low- to intermediate-risk MDS; AND
C) According to the prescriber the patient has clinically-significant thrombocytopenia (e.g., low platelet counts [< 30 x 10^9/L {< 30,000/µL} {pretreatment}]; is platelet transfusion-dependent; active bleeding, and/or a history of bleeding at low platelet counts).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Promacta has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Promacta® tablets and oral suspension [prescribing information]. East Hanover, NJ: Novartis; April 2019.
2. Killick SB Bown N, Cavenagh J, et al, on behalf of the British Society for Standards in Hematology. Guidelines for the diagnosis and management of adult aplastic anaemia. *Br J Haematol*. 2016;172:187-207.
3. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117:4190-4207.
4. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (Version 2.2019 – October 18, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 30, 2019.
5. Platzbecker U, Wong RS, Verma A, et al. Safety and tolerability of eltrombopag versus placebo for treatment of thrombocytopenia in patients with advanced myelodysplastic syndromes or acute myeloid leukemia: a multicenter, randomized, placebo-controlled, double-blind, phase 1/2 trial. *Lancet Haematol*. 2015;2(10):e417-26.
6. Olivia EN, Alati C, Santini V, et al. Eltrombopag versus placebo for lower-risk myelodysplastic syndromes with thrombocytopenia (EQol-MDS): phase 1 results for a single-blind, randomized, controlled phase 2 superiority trial. *Lancet Haematol*. 2017;4(3):e127-e136.
7. Brierley CK, Steensma DP. Thrombopoiesis-stimulating agents and myelodysplastic syndromes. *Br J Haematol*. 2015;169:309-323.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	The name of the policy was changed to add the header "Thrombopoietin Receptor Agonists". The diagnosis of thrombocytopenia in MDS was removed from the "Conditions Not Recommended for Approval" section and added to the "Other Uses with Supportive Evidence". Criteria are to approve for 12 months if the agent is prescribed by, or in consultation with, a hematologist or an oncologist; if the patient has low- to intermediate-risk MDS; and if, according to the prescribing physician, the patient has clinically significant thrombocytopenia (examples listed).	06/14/2017
Annual revision	The wording of the diagnosis of ITP was changed from "Treatment of Thrombocytopenia in Patients with Chronic Immune (Idiopathic) Thrombocytopenia Purpura" to "Chronic Immune Thrombocytopenia". Also, for chronic ITP, the wording regarding medication trials was changed. Previously, patients were required to meeting one of the following conditions: 1) the patient has tried corticosteroids; 2) the patient has tried IVIG; OR 3) the patient has undergone splenectomy. This criteria wording was changed to state that the patient meets one of the following criteria: 1) the patient has tried one other therapy (e.g., corticosteroids, IVIG, anti-D immunoglobulin, Nplate, Tavalisse, or Rituxan) OR 2) the patient has undergone splenectomy.	06/27/2018
Selected revision	Criteria added regarding aplastic anemia for its new indication. The additional criterion added was to also permit approval if the patient will be using Promacta in combination with standard immunosuppressive therapy (e.g., cyclosporine, Atgam® [lymphocyte immune globulin, anti-thymocyte globulin [equine] sterile solution for intravenous use only], mycophenolate moefetil, or sirolimus).	12/05/2018
Annual revision	The following criteria changes were made: **1. Chronic Immune Thrombocytopenia:** Doptelet was added to the list of alternatives that count towards the criteria that requires a trial of one other therapy. The approval duration was changed from 3 years to 1 year.	07/03/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee; MDS – Myelodysplastic syndrome; ITP – Immune thrombocytopenia; IVIG – Intravenous immunoglobulin.