PRIOR AUTHORIZATION POLICY

POLICY: Thrombocytopenia – Promacta Prior Authorization Policy
- Promacta® (eltrombopag tablets and oral suspension – Novartis)

REVIEW DATE: 04/12/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Promacta, a thrombopoietin receptor agonist, is indicated for the following uses:[1]

- **Aplastic anemia**, severe, in combination with standard immunosuppressive therapy for the first-line treatment of adults and pediatric patients ≥ 2 years of age as well as for treatment in patients who have had an insufficient response to immunosuppressive therapy.
- **Chronic hepatitis C, treatment of thrombocytopenia**, to allow the initiation and maintenance of interferon-based therapy.
- **Immune thrombocytopenia (ITP), treatment, in adults and pediatric patients ≥ 1 year of age** with persistent or chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Of note, Promacta should only be used in patients whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.

For patients with refractory severe aplastic anemia, if no hematologic response has occurred after 16 weeks of treatment with Promacta, discontinue therapy. For ITP, Promacta should be discontinued if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks of therapy with Promacta at the maximum daily dose of 75 mg. Use Promacta only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy.[1]

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. For the management of chronic hepatitis C, Promacta should be stopped upon discontinuation of antiviral treatment futility.

Guidelines

Promacta is addressed in several guidelines.

- **Aplastic Anemia:** Guidelines for the diagnosis and management of adults with aplastic anemia are available from the British Society for Standards in Hematology (2016).[2] 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 between 35 to 50 years of age. Other recommended immunosuppressives 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).
- **Immune Thrombocytopenia (ITP):** In 2019, the American Society of Hematology updated guidelines for ITP.[3] There are several recommendations. For adults with ITP for at least 3 months who are corticosteroid-dependent or unresponsive to corticosteroid, a thrombopoietin receptor agonist (Promacta or Nplate® [romiplostim subcutaneous injection]) or a splenectomy are recommended. In children with newly diagnosed ITP who have non-life-threatening mucosal bleeding, corticosteroids are recommended. For children who have non-life-threatening mucosal bleeding and did not respond to first-line treatment, thrombopoietin receptor agonists are recommended. Other treatment options in children and adults include intravenous immunoglobulin, anti-D immunoglobulin, and rituximab.
- **Myelodysplastic Syndrome (MDS):** Recommendations from the National Comprehensive Cancer Network for MDS (version 1.2023 – September 12, 2022) state that treatment with a thrombopoietin receptor agonist should be considered in patients with lower-risk MDS who have severe or life-threatening thrombocytopenia.[4] The data with Promacta are discussed noting an increased rate of platelet response and decreased overall bleeding events in patients with low- to intermediate-risk MDS. Other data are also 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. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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 long-term efficacy, approval requires Promacta to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Promacta® (eltrombopag tablets and oral suspension (Novartis) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

FDA-Approved Indications

1. **Aplastic Anemia.** Approve if the patient meets one of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets the following criteria (i, ii, and iii):
     - **i.** Patient has low platelet counts at baseline (pretreatment); AND
       Note: An example of a low platelet count is < 30 x 10^9/L (< 30,000/mcL).
     - **ii.** Patient meets one of the following criteria (a or b):
       - **a)** Patient had tried at least one immunosuppressant therapy; OR
         Note: Examples of therapies are cyclosporine, Atgam (lymphocyte immune globulin, anti-thymocyte globulin [equine] sterile solution for intravenous use only), mycophenolate mofetil, or sirolimus.
       - **b)** Patient will be using Promacta in combination with standard immunosuppressive therapy; AND
         Note: Examples of therapies are cyclosporine, Atgam (lymphocyte immune globulin, anti-thymocyte globulin [equine] sterile solution for intravenous use only), mycophenolate mofetil, or sirolimus.
     - **iii.** Promacta is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving Promacta. Approve for 1 year if, according to the prescriber, the patient demonstrates a beneficial clinical response.
     Note: Examples include increases in platelet counts, reduction in red blood cell transfusions, hemoglobin increase, and/or absolute neutrophil count increase.

2. **Immune Thrombocytopenia.** Approve if the patient meets one of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** Patient meets one of the following criteria (a or b):
       - **a)** Patient has a platelet count < 30 x 10^9/L (< 30,000/mcL); OR
       - **b)** Patient meets both of the following criteria [(1) and (2)]:
         - **(1)** Patient has a platelet count < 50 x 10^9/L (< 50,000/mcL); AND
         - **(2)** According to the prescriber the patient is at an increased risk for bleeding; AND
     - **ii.** Patient meets one of the following criteria (a or b):
       - **a)** Patient has tried at least one other therapy; OR

Note: Examples of therapies are systemic corticosteroids, intravenous immunoglobulin, anti-D immunoglobulin, Nplate (romiplostim subcutaneous injection), Tavalisse (fostamatinib tablets), Doptelet (avatrombopag tablets), or rituximab.

b) Patient has undergone splenectomy; AND

iii. The medication is prescribed by or in consultation with a hematologist; OR

B) Patient is Currently Receiving Promacta. Approve for 1 year if the patient meets both of the following criteria (i and ii):

i. According to the prescriber, the patient demonstrates a beneficial clinical response; AND

Note: A beneficial response can include increased platelet counts, maintenance of platelet counts, and/or a decreased frequency of bleeding episodes.

ii. Patient remains at risk for bleeding complications.

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

A) Patient has low platelet counts at baseline (pretreatment); AND
Note: An example of a low platelet count is < 75 x 10^9/L (< 75,000/mcL).

B) Patient will be receiving interferon-based therapy for chronic hepatitis C; AND
Note: Examples of therapies are pegylated interferon (Pegasys [peginterferon alfa-2a injection], PegIntron [peginterferon alfa-2b injection]), or Intron A (interferon alfa-2b).

C) The medication is prescribed by or in consultation with a gastroenterologist, a hepatologist, or a physician who specializes in infectious disease.

Other Uses with Supportive Evidence

4. Thrombocytopenia in a Patient with Myelodysplastic Syndrome. Approve if the patient meets one of the following criteria (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i, ii, and, iii):

i. Patient has low- to intermediate-risk myelodysplastic syndrome; AND

ii. Patient meets one of the following criteria (a or b):

a) Patient has a platelet count < 30 x 10^9/L (< 30,000/mcL); OR

b) Patient meets one of the following criteria [(1) and (2)]:

(1) Patient has a platelet count < 50 x 10^9/L (< 50,000/mcL); AND

(2) According to the prescriber, the patient is at an increased risk for bleeding; AND

iii. The medication is prescribed by or in consultation with a hematologist or an oncologist; OR

B) Patient is Currently Receiving Promacta. Approve for 1 year if the patient meets both of the following criteria (i and ii):

i. According to the prescriber, the patient demonstrates a beneficial clinical response; AND

Note: A beneficial response can include increased platelet counts, maintenance of platelet counts, and/or decreased frequency of bleeding episodes.

ii. Patient remains at risk for bleeding complications.

CONDITIONS NOT COVERED

- **Promacta® (eltrombopag tablets and oral suspension (Novartis) is(are) considered experimental, investigational or unproven for ANY other use(s).**

REFERENCES

1. Promacta® tablets and oral suspension [prescribing information]. East Hanover, NJ: Novartis; March 2023.
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, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829-3866.
4. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (Version 1.2023 – September 12, 2022). © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed April 6, 2023.
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	Review Date
Annual Revision	**Aplastic Anemia:** The wording of "Continuation of Therapy" was changed to "Patient is Currently Receiving Promacta." **Immune Thrombocytopenia:** The wording of "Continuation of Therapy" was changed to "Patient is Currently Receiving Promacta." **Thrombocytopenia in Myelodysplastic Syndrome:** The wording of "Continuation of Therapy" was changed to "Patient is Currently Receiving Promacta."	03/23/2022
Annual Revision	No criteria changes.	04/12/2023