Drug Coverage Policy

Effective Date.....07/15/2024
Coverage Policy Number.....IP0153
Policy Title.....Eltrombopag Products

Thrombocytopenia – Eltrombopag Products

- Alvaiz™ (eltrombopag choline tablets – Teva)
- Promacta® (eltrombopag olamine tablets and oral suspension – Novartis)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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.

Alvaiz, a thrombopoietin receptor agonist, is indicated for the following uses:[2]

- **Aplastic anemia**, severe, in adults who have had an insufficient response to immunosuppressive therapy.
- **Chronic hepatitis C, treatment of thrombocytopenia**, in adults to allow the initiation and maintenance of interferon-based therapy.
- **ITP, treatment, in adults and pediatric patients ≥ 6 year of age** with persistent or chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Of note, Alvaiz 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 eltrombopag, discontinue therapy. For ITP, eltrombopag 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 eltrombopag at the maximum daily dose. Use eltrombopag 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 eltrombopag 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, eltrombopag should be stopped upon discontinuation of antiviral treatment futility.

Guidelines

Eltrombopag 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 (2024).[3] Standard treatment for newly diagnosed acquired aplastic anemia is anti-thymocyte globulin (ATG)-based immunosuppressive therapy with eltrombopag or allogeneic hematopoietic stem cell transplantation (HSCT) from a matched sibling donor. The current standard first-line immunosuppressive therapy is horse ATG combined with cyclosporine, but horse ATG-ATAGAM with cyclosporine and eltrombopag should be recommended. Eltrombopag 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.[4] 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 (eltrombopag 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 (NCCN) for MDS (version 1.2024 – February 12, 2024) state that treatment with a thrombopoietin receptor agonist should be considered in patients with lower-risk MDS who have significant, severe, life-threatening, or refractory thrombocytopenia.[5] The data with eltrombopag 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 eltrombopag in patients with MDS.[6-8]

- **Thrombocytopenia in a Patient Post-Allogeneic Transplantation:** Recommendations from the NCCN for Hematopoietic Growth Factors (version 3.2024 – January 30, 2024) state to consider eltrombopag for the treatment of prolonged thrombocytopenia in patients post-allogeneic transplant and poor graft function (category 2A).[9] Other data are also available that describe the use of eltrombopag in this clinical scenario.[10-17]

Medical Necessity Criteria

I. Promacta is considered medically necessary when ONE of the following is met:

FDA-Approved Indications

1. **Aplastic Anemia.** Approve if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets ALL of the following (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 (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 eltrombopag 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.** The medication is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving Eltrombopag. 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 (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient meets ONE of the following (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 (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 (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), and 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 Eltrombopag. Approve for 1 year if the patient meets BOTH of the following (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 ALL of the following (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 (A or B):
   A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
   i. Patient has low- to intermediate-risk myelodysplastic syndrome; AND
   ii. Patient meets ONE of the following (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 (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 Eltrombopag. Approve for 1 year if the patient meets BOTH of the following (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.

5. **Thrombocytopenia in a Patient Post-Allogeneic Transplantation**. Approve if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 3 months if the patient meets ALL the following (i, ii, and, iii):
   i. According to the prescriber, the patient has poor graft function; AND
   ii. Patient has a platelet count < 50 x 10^9/L (< 50,000/mcL); AND
   iii. The medication is prescribed by or in consultation with a hematologist, an oncologist, or a stem cell transplant specialist physician; OR
   B) Patient is Currently Receiving Eltrombopag. Approve for 6 months if according to the prescriber, the patient demonstrated a beneficial clinical response.

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

II. Alvaiz is considered medically necessary when ONE of the following is met:

FDA-Approved Indications

1. **Aplastic Anemia.** Approve if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** 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).
     - **iii.** Patient meets ONE of the following (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 eltrombopag 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.
     - **iv.** The medication is prescribed by or in consultation with a hematologist; OR
     - **v.** Preferred product criteria is met for the product(s) as listed in the below table(s)
   - **B)** Patient is Currently Receiving Eltrombopag. 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 (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient meets ONE of the following (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 (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.** Patient meets ONE of the following (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
     - **iv.** The medication is prescribed by or in consultation with a hematologist; OR
     - **v.** Preferred product criteria is met for the product(s) as listed in the below table(s)
   - **B)** Patient is Currently Receiving Eltrombopag. Approve for 1 year if the patient meets BOTH of the following (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 ALL of the following (A, B, C, D, and E):
   A) Patient is ≥ 18 years of age; AND
   B) 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).
   C) 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).
   D) The medication is prescribed by or in consultation with a gastroenterologist, a hepatologist, or a physician who specializes in infectious disease.
   E) Preferred product criteria is met for the product(s) as listed in the below table(s)

Other Uses with Supportive Evidence

4. **Thrombocytopenia in a Patient with Myelodysplastic Syndrome.** Approve if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, and iv):
      i. Patient has low- to intermediate-risk myelodysplastic syndrome; AND
      ii. Patient meets ONE of the following (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 (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
      iv. Preferred product criteria is met for the product(s) as listed in the below table(s)
   B) Patient is Currently Receiving Eltrombopag. Approve for 1 year if the patient meets BOTH of the following (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.

5. **Thrombocytopenia in a Patient Post-Allogeneic Transplantation.** Approve if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 6 months if the patient meets ALL the following (i, ii, iii, and iv):
      i. According to the prescriber, the patient has poor graft function; AND
      ii. Patient has a platelet count < 50 x 10^9/L (< 50,000/mcL); AND
      iii. The medication is prescribed by or in consultation with a hematologist, an oncologist, or a stem cell transplant specialist physician; OR
      iv. Preferred product criteria is met for the product(s) as listed in the below table(s)

B) Patient is Currently Receiving Eltrombopag. Approve for 6 months if according to the prescriber, the patient demonstrated a beneficial clinical response.
Note: A beneficial response can include increased platelet counts, maintenance of platelet counts, and/or decreased frequency of bleeding episodes.

Employer Plans:

Product	Criteria
Alvaiz (eltrombopag choline) tablets	**ONE** of the following (1 or 2): **1.** Patient has tried Promacta [may require prior authorization] **2.** Patient has already been started on therapy with Alvaiz

Individual and Family Plans:

Product	Criteria
Alvaiz (eltrombopag choline) tablets	**ONE** of the following (1 or 2): **1.** Patient has tried Promacta [may require prior authorization] **2.** Patient has already been started on therapy with Alvaiz

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

References

1. Promacta® tablets and oral suspension [prescribing information]. East Hanover, NJ: Novartis; March 2023.
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3. Kulasekararaj A, Cavenagh J, Dokal I, et al, on behalf of the British Society of Hematology. Guidelines for the diagnosis and management of adult aplastic anaemia: a British Society for Haematology Guideline. *Br J Haematol*. 2024 Jan 21. [Online ahead of print].
4. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829-3866.
5. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (Version 1.2024 – February 12, 2024). © 2024 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 18, 2024.
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7. 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.
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12. Yuan C, Boyd AM, Nelson J, et al. Eltrombopag for treating thrombocytopenia after allogeneic stem cell transplantation. *Biol Blood Marrow Transplant*. 2019;25:1320-1324.
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Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	Alvaiz (eltrombopag choline tablets) added to the policy. **Promacta (Aplastic Anemia)** **Added** examples of a beneficial response to the Patient is Currently Receiving Eltrombopag approach. **Promacta (Immune Thrombocytopenia)** **Removed** the age restriction. **Removed** contraindication or intolerance to ALL therapies. **Added** examples of a beneficial response to the Patient is Currently Receiving Eltrombopag approach. **Promacta (Thrombocytopenia in a Patient with Myelodysplastic Syndrome)**	07/15/2024

	Added examples of a beneficial response to the Patient is Currently Receiving Eltrombopag approach. **Added** Promacta coverage for Thrombocytopenia in a Patient Post-Allogeneic Transplantation.	

The policy effective date is in force until updated or retired.