PRIOR AUTHORIZATION POLICY

POLICY: Thrombocytopenia – Eltrombopag Products Prior Authorization Policy
- Alvaiz™ (eltrombopag choline tablets – Teva)
- Promacta® (eltrombopag olamine tablets and oral suspension – Novartis)

REVIEW DATE: 04/24/2024

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]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of eltrombopag products. 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 eltrombopag products as well as the monitoring required for adverse events and long-term efficacy, approval may require eltrombopag products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

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]), and 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 diseases.

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 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. Coverage of Alvaiz is recommended in those who meet ONE of the following criteria:

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, and iv):

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, and 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, and sirolimus.

iv. 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, iii, and iv):

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), and rituximab.
b) Patient has undergone splenectomy; AND

iv. 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, C, and D):
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]), and 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 diseases.

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 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 6 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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Promacta or Alvaiz is not recommended in the following situations:

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; March 2023.
2. Alvaiz™ tablets [prescribing information]. Parsippany, NJ: Teva; November 2023.
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.
6. 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.
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.
8. Oliva EN, Riva M, Miscola P, et al. Eltrombopag for low-risk myelodysplastic syndrome with thrombocytopenia: interim results of a Phase II, randomized, placebo-controlled clinical trial (EQOL-MDS). *J Clin Oncol*. 2023;41(28):4486-4496.
9. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (Version 3.2024 – January 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 18, 2024.
10. Gao F, Zhou X, Shi J, et al. Eltrombopag treatment promotes platelet recovery and reduces platelet transfusion for patients with post-transplantation thrombocytopenia. *Ann Hematol*. 2020;99:2679-2687.
11. Marotta S, Marano L, Ricci P, et al. Eltrombopag for post-transplant cytopenias due to poor graft function. *Bone Marrow Transplant*. 2019;54:1346-1353.
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.
13. Halahleh K, Gale RP, Da'na W, et al. Therapy of posttransplant poor graft function with eltrombopag. *Bone Marrow Transplant*. 2021;56:4-6.
14. Aydin S, Dellacasa C, Manetta S, et al. Rescue treatment with eltrombopag in refractory cytopenias after allogeneic stem cell transplantation. *Ther Adv Hematol*. 2020;11:2040620720961910.
15. Shahzad M, Iqbal Q, Munir F, et al. Outcomes with eltrombopag for poor graft function following allogeneic hematopoietic stem cell transplantation: a systematic review and meta-analysis. *Blood*. 2022;140:12846-12847.
16. Ahmed S, Bashir Q, Bassett R, et al. Eltrombopag for post-transplantation thrombocytopenia: results of phase II randomized, double-blind, placebo-controlled trial. *Transplant Cell Ther*. 2021;27:430.e1-430.e7.
17. Gunes EK, Kaya SY, Yaman F, et al. Eltrombopag treatment in thrombocytopenia following hematopoietic stem cell transplantation: a multicenter real world analysis. *Leuk Res*. 2024;140:107484.