BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.85.015

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Hematological Agents	**Original Policy Date:**	May 3, 2013
Subject:	Promacta Alvaiz	**Page:**	1 of 9

Last Review Date: June 13, 2024

Promacta Alvaiz

Description

Promacta, Alvaiz (eltrombopag)

Background
Promacta and Alvaiz are used to treat patients with chronic immune thrombocytopenia (ITP), who have not responded adequately to corticosteroids, immunoglobulins, or to the removal of their spleen (splenectomy). ITP is a blood disorder that results in a low number of platelets which can lead to serious bleeding. Promacta and Alvaiz work by stimulating the bone marrow to produce needed platelets (1-2).

Regulatory Status
FDA-approved indications (1-2):

1. **Promacta** is a thrombopoietin receptor agonist indicated for the treatment of:
    a. Thrombocytopenia in adult and pediatric patients 1 year and older with persistent or chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
    b. Thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy
    c. Patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy
    d. In combination with standard immunosuppressive therapy for first line treatment of adult and pediatric patients 2 years and older with severe aplastic anemia
2. **Alvaiz** is a thrombopoietin receptor agonist indicated for the treatment of:

a. Thrombocytopenia in adult and pediatric patients 6 years and older persistent or chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
b. Thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy
c. Adult patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy

Limitations of Use: (1-2)

1. Promacta and Alvaiz should not be used to normalize platelet counts.
2. Promacta and Alvaiz should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
3. Promacta and Alvaiz should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon therapy or limits the ability to maintain optimal interferon-based therapy.
4. Promacta and Alvaiz are not indicated for the treatment of patients with myelodysplastic syndrome (MDS).
5. Safety and efficacy have not been established in combination with direct acting antiviral agents approved for treatment of chronic hepatitis C infection.

Promacta and Alvaiz carry boxed warnings regarding the risk for hepatic decompensation in patients with chronic hepatitis C and risk of hepatotoxicity. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels must be measured prior to initiation of Promacta and Alvaiz, every 2 weeks during the dose adjustment phase, and monthly following establishment of a stable dose. Monitor serum liver tests weekly until the abnormality/abnormalities resolve, stabilize, or return to baseline levels. Promacta and Alvaiz should be discontinued for the development of important liver test abnormalities. Promacta and Alvaiz, in combination with interferon and ribavirin in patients with chronic hepatitis C, may increase the risk of hepatic decompensation (1-2).

Promacta and Alvaiz must be discontinued if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks of therapy at the maximum daily dose. Discontinue if ALT levels increase to ≥3X upper limit of normal (ULN) in patients with normal liver function or ≥3X baseline in patients with pre-treatment elevations in transaminases and are: 1) progressive 2) persistent for ≥4 weeks 3) accompanied by increased direct bilirubin, or 4) accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation. Promacta and Alvaiz should be discontinued when antiviral therapy is discontinued (1-2).

Promacta and Alvaiz must be held when platelet levels reach >400 x 10^9/L and platelet levels monitored twice weekly to evaluate any decrease in levels and need for re-initiation of therapy. If platelet levels remain above 400 x 10^9/L after two weeks, therapy must be discontinued. If platelet count drops to <150 x 10^9/L, therapy can be restarted at a decreased dose (1-2).

Thrombotic/thromboembolic complications may result from increases in platelet counts with Promacta and Alvaiz. There is an increased risk of thromboembolism when administering Promacta and Alvaiz to patients with known risk factors (e.g., Factor V Leiden, ATIII deficiency, antiphospholipid syndrome, chronic liver disease). To minimize the risk for thrombotic/thromboembolic complications, do not use Promacta or Alvaiz in an attempt to normalize platelet counts (1-2).

During the dose adjustment phase of therapy, complete blood counts (CBCs) with differentials (including platelet counts) should be obtained weekly then monthly after stabilization of dose, then weekly for 4 weeks after discontinuation of therapy (1-2).

The safety and efficacy of Promacta in pediatric patients less than 1 year of age with chronic ITP have not been established. The safety and efficacy of Promacta in patients less than 2 years of age with severe aplastic anemia has not been established. The safety and efficacy of Promacta and Alvaiz in pediatric patients with thrombocytopenia associated with chronic hepatitis C have not been established. The safety and efficacy of Alvaiz in pediatric patients less than 6 years of age with chronic ITP have not been established. The safety and efficacy of Alvaiz in pediatric patients with severe aplastic anemia have not been established (1-2).

Related policies
Cablivi

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Promacta and Alvaiz may be considered **medically necessary** if the conditions indicated below are met.

Promacta and Alvaiz may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses
Promacta only

Patient must have **ONE** of the following:

1. Chronic or persistent immune (idiopathic) thrombocytopenia (ITP)
    a. 1 year of age or older
    b. Inadequate response or intolerant to corticosteroids, immunoglobulins, or splenectomy
    c. Platelet count at time of diagnosis less than 50,000 platelets per microliter

2. Thrombocytopenia associated with chronic hepatitis C
    a. 18 years of age or older
    b. Used to initiate and maintain interferon-based therapy
    c. Platelet count at time of diagnosis less than 75,000 platelets per microliter

3. Severe aplastic anemia
    a. 18 years of age or older
    b. Inadequate response to immunosuppressive therapy
    c. Platelet count at time of diagnosis less than 50,000 platelets per microliter

OR

    a. 2 years of age or older
    b. First line therapy in combination with standard immunosuppressive therapy
    c. Platelet count at time of diagnosis less than 50,000 platelets per microliter

AND ALL of the following for **ALL** indications:

1. Prescriber agrees to obtain baseline clinical hematology and liver function tests and to monitor during treatment
2. **NOT** used in combination with another thrombopoietin receptor agonist or with Tavalisse (fostamatinib disodium hexahydrate)

Diagnoses
Alvaiz only

Patient must have **ONE** of the following:

1. Chronic or persistent immune (idiopathic) thrombocytopenia (ITP)
    a. 6 years of age or older
    b. Inadequate response or intolerant to corticosteroids, immunoglobulins, or splenectomy.
    c. Platelet count at time of diagnosis less than 50,000 platelets per microliter

2. Thrombocytopenia associated with chronic hepatitis C
    a. 18 years of age or older
    b. Used to initiate and maintain interferon-based therapy
    c. Platelet count at time of diagnosis less than 75,000 platelets per microliter

3. Severe aplastic anemia
    d. 18 years of age or older
    e. Inadequate response to immunosuppressive therapy
    f. Platelet count at time of diagnosis less than 50,000 platelets per microliter

AND ALL of the following for **ALL** indications:

1. Prescriber agrees to obtain baseline clinical hematology and liver function tests and to monitor during treatment
2. **NOT** used in combination with another thrombopoietin receptor agonist or with Tavalisse (fostamatinib disodium hexahydrate)

Prior – Approval *Renewal* Requirements

Diagnoses
Promacta only

Patient must have **ONE** of the following:

1. Chronic or persistent immune (idiopathic) thrombocytopenia (ITP)
    a. 1 year of age or older

2. Thrombocytopenia associated with chronic hepatitis C

a. 18 years of age or older
b. Used to maintain interferon-based therapy

3. Severe aplastic anemia
    a. 2 years of age or older
    b. **Age 2-17 only:** used in combination with standard immunosuppressive therapy

AND ONE of the following for **ALL** indications:

1. Platelet count 50,000 platelets per microliter to 200,000 platelets per microliter
2. Platelet count ≥ 200,000 platelets per microliter to ≤ 400,000 platelets per microliter: prescriber agrees that therapy will be adjusted to the minimum platelet count needed to reduce the bleeding risk

AND ALL of the following for **ALL** indications:

1. Prescriber agrees to monitor clinical hematology and liver function tests during treatment
2. ALT counts < 3 times the upper limit of normal
3. **NOT** used in combination with another thrombopoietin receptor agonist or with Tavalisse (fostamatinib disodium hexahydrate)

Diagnoses
Alvaiz only

Patient must have **ONE** of the following:

1. Chronic or persistent immune (idiopathic) thrombocytopenia (ITP)
    a. 6 years or age or older

2. Thrombocytopenia associated with chronic hepatitis C
    a. 18 years of age or older
    b. Used to maintain interferon-based therapy

3. Severe aplastic anemia
    a. 18 years or age or older

AND ONE of the following for **ALL** indications:

1. Platelet count 50,000 platelets per microliter to 200,000 platelets per microliter
2. Platelet count ≥ 200,000 platelets per microliter to ≤ 400,000 platelets per microliter: prescriber agrees that therapy will be adjusted to the minimum platelet count needed to reduce the bleeding risk

AND ALL of the following for **ALL** indications:

1. Prescriber agrees to monitor clinical hematology and liver function tests during treatment
2. ALT counts < 3 times the upper limit of normal
3. **NOT** used in combination with another thrombopoietin receptor agonist or with Tavalisse (fostamatinib disodium hexahydrate)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Promacta and Alvaiz are indicated for the treatment of thrombocytopenia in patients with persistent or chronic immune (idiopathic) thrombocytopenia (ITP), thrombocytopenia in patients with chronic hepatitis C, and severe aplastic anemia. The safety and efficacy of Promacta in pediatric patients less than 1 year of age with chronic ITP have not been established. The safety and efficacy of Promacta in patients less than 2 years of age with severe aplastic anemia has not been established. The safety and efficacy of Promacta and Alvaiz in pediatric patients with thrombocytopenia associated with chronic hepatitis C have not been established. The safety and efficacy of Alvaiz in pediatric patients less than 6 years of age with chronic ITP have not been established. The safety and efficacy of Alvaiz in pediatric patients with severe aplastic anemia have not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Promacta and Alvaiz while maintaining optimal therapeutic outcomes.

References

1. Promacta [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2023.
2. Alvaiz [package insert]. Parsippany, NJ: Teva Pharmaceuticals; November 2023.

Policy History

Date	Action
May 2013	Addition to PA
September 2014	Annual criteria review and reference update Removal of agreement to stop Promacta therapy upon discontinuation of antiviral therapy and monitor platelet counts every week prior to starting antiviral therapy and not used in combination with direct acting antiviral agents Addition of new indication – severe aplastic anemia
July 2015	Change in age requirement for chronic or persistent ITP from 18 to 6 yrs of age
August 2015	Change in age requirement for chronic or persistent ITP from 6 to 1 yrs of age
December 2016	Annual editorial review and reference update Policy code changed from 5.10.15 to 5.85.15
September 2017	Annual editorial review and reference update
September 2018	Annual editorial review and reference update Verbiage for platelet count changed from 10^9/L to number of platelets per microliter Verbiage of ALT count changed from ULN to upper limit of normal Addition of no dual therapy with another thrombopoietin receptor agonist or with Tavalisse (fostamatinib disodium hexahydrate) to criteria
November 2018	Addition of new indication: severe aplastic anemia in patients 2 years of age and older as first line therapy in combination with standard immunosuppressive therapy
March 2019	Annual review
June 2019	Annual review
September 2020	Annual review and reference update
September 2021	Annual review and reference update
September 2022	Annual review and reference update
June 2023	Annual review and reference update
March 2024	Annual review

April 2024	Addition of Alvaiz to policy. Reworded monitoring requirements
June 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.