09-J3000-00

Original Effective Date: 06/15/18

Reviewed: 12/11/24

Revised: 01/15/25

Subject: Fostamatinib (Tavalisse)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Fostamatinib (Tavalisse®) is a tyrosine kinase inhibitor with activity against spleen tyrosine kinase (Syk). Hematopoietic cells such as macrophages, B cells, T cells, and platelets express Syk. When Syk is activated by Fc receptors binding to ligands, it can cause downstream signaling that results in cytoskeletal rearrangements, phagocytosis and proinflammatory effects. Fostamatinib reduces antibody-mediated destruction of platelets by blocking activation of Syk. In April 2018, the US Food and Drug Administration (FDA) approved fostamatinib for treatment of thrombocytopenia in adults with chronic immune thrombocytopenia purpura (ITP) who have had an insufficient response to a previous treatment.

ITP is an autoimmune disorder characterized by a destruction of otherwise normal platelets and frequently occurs without a known or identifiable cause; it is considered a diagnosis of exclusion as there are no diagnostic tests to confirm ITP. The American Society of Hematology (ASH) published a guideline outlining the diagnosis and management of ITP. Treatment of newly diagnosed ITP is recommended when the platelet count is less than 30,000. Initial treatment options for ITP include corticosteroids, IVIG, or anti-D.

Persons who are unresponsive to or relapse after initial corticosteroid therapy are considered to have chronic ITP. In this setting, the following treatment options are recommended:

- Splenectomy
- Thrombopoietin receptor agonists (e.g., eltrombopag [Promacta] or romiplostim [Nplate])
- Rituximab (Rituxan)

The clinical efficacy and safety of fostamatinib was evaluated in two identical double-blind, placebo-controlled studies. Patients with persistent or chronic ITP who had an insufficient response to previous treatment [corticosteroids (94%), immunoglobulins (53%), splenectomy (35%), and/or a thrombopoietin

receptor agonist (48%)] were included and randomized 2:1 to receive fostamatinib or placebo for 24 weeks. Stable use of concurrent ITP medications (glucocorticoids, azathioprine or danazol) and rescue therapy was permitted. The median baseline platelet count was 16 x 10^9/L and 47% of patients were receiving stable ITP medications. The main efficacy outcome was defined as a stable platelet response of at least 50 x 10^9/L on at least 4 of 6 visits between weeks 14 to 24. In the first trial, 9 (18%) patients achieved a stable platelet response in the fostamatinib group as compared to 0 in the placebo group (p = 0.03). In the second trial, 8 (16%) patients achieved a stable platelet response in the fostamatinib group as compared to 1 (4%) in the placebo (p = not significant). In both trials, rescue medication was required by 30% and 45% patients receiving fostamatinib and placebo, respectively. The incidence of bleeding occurred in 29% and 37% of patients receiving fostamatinib and placebo, respectively. Severe bleeding leading to hospitalization occurred in 1 (1%) patient receiving fostamatinib as compared to 3 (6%) receiving placebo. Of the 47 patients enrolled in either trial who had previously received a thrombopoietin receptor agonist, 8 (17%) patients received a stable response. Patients who did not respond to treatment after 12 weeks or who completed trial 1 or 2 at 24 weeks were eligible for an open label extension trial. A total of 18 patients maintained a stable platelet count (at least 50 x 10^9/L) for at least 12 months or longer who were enrolled in trial 1 or 2, or the open label extension. The most common adverse reactions in patients receiving fostamatinib included diarrhea, hypertension, and nausea.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

I. Initiation of fostamatinib (Tavalisse®) **meets the definition of medical necessity** when used to treat thrombocytopenia associated with **ANY** of the following conditions:

   A. Chronic immune (idiopathic) thrombocytopenic purpura (ITP) and **ALL** of the following are met:

      1. The member has demonstrated an insufficient response to **ONE or more** of the following:

         a. Adequate trial of corticosteroids (e.g., prednisone 1-2 mg/kg for 2-4 weeks)

         b. Immunoglobulins therapy (e.g., intravenous immune globulin [IVIG])

         c. Thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Promacta], avatrombopag [Doptelet])

      2. **ONE** of the following:

         a. The member's platelet count is less than 30,000

         b. The member has symptomatic bleeding or increased risk for bleeding and platelet count is less than 50,000

3. Fostamatinib is not used concurrently with chronic immune globulin therapy, rituximab, or a thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Alvaiz, Promacta], avatrombopag [Doptelet], lusutrombopag [Mulpleta])
4. The dosage does not exceed 300 mg daily and will be achieved using the fewest number of tablets per day.

Approval duration: 6 months

II. Continuation of therapy fostamatinib (Tavalisse®) **meets the definition of medical necessity** when used for the treatment of thrombocytopenia associated with chronic ITP and **ALL** of the condition-specific criteria are met:

A. Chronic ITP

1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for fostamatinib for the treatment of chronic ITP, **OR** the member has previously met all indication-specific criteria
2. The member has a beneficial response to therapy evidenced by an improvement in platelet count from baseline – documentation must be submitted
3. Fostamatinib is not used concurrently with chronic immune globulin therapy, rituximab, or a thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Alvaiz, Promacta], avatrombopag [Doptelet], lusutrombopag [Mulpleta])
4. The dose does not exceed 300 mg daily and will be achieved using the fewest number of tablets per day.

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Thrombocytopenia associated with chronic ITP in adults who have had an insufficient response to a previous treatment: 100 mg orally twice daily. After a month, if platelet count has not increased above 50 x 10^9/L, increase dose to 150 mg twice daily. Discontinue after 12 weeks if the platelet count does not increase to a level sufficient to avoid clinically important bleeding. After obtaining baseline assessments, monitor complete blood counts including platelets and neutrophils, liver function tests, and blood pressure regularly.

Dose Adjustments

Adverse reactions:

- Dose reduction, temporary interruption of therapy or discontinuation may be necessary for management of specific adverse reactions. If a dose reduction is necessary, titrate to a lower dosage according to prescribing information. The lowest recommended dose is 100 mg daily. See prescribing information for dose specific recommendations and supportive care due to hypertension, hepatotoxicity, diarrhea, and neutropenia.

CYP3A4 inhibitors:

- Concomitant use with a strong CYP3A4 inhibitor increases exposure to the major active metabolite of fostamatinib. Monitor for toxicities that may require dose modification if given concurrently with a strong CYP3A4 inhibitor.

CYP3A4 inducers:

- Concomitant use with strong CYP3A4 inducers is not recommended.

Drug Availability

- 100 mg and 150 mg tablets

PRECAUTIONS:

Boxed Warning

Contraindications

- None

Precautions/Warnings

- Hypertension: monitor blood pressure every 2 weeks until stable then monthly. Manage hypertension using standard antihypertensive treatment and interrupt, reduce, or discontinue fostamatinib if necessary.
- Hepatotoxicity: monitor LFTs monthly. If LFT levels are elevated, interrupt, reduce, or discontinue fostamatinib if necessary.
- Diarrhea: manage diarrhea with supportive measures. If severe, interrupt, reduce, or discontinue fostamatinib if necessary.
- Neutropenia: Monitor ANC monthly and for infection. If neutrophil count decreases below 1.0 x 10^9/L, interrupt, reduce, or discontinue fostamatinib if necessary.
- Embryo-fetal toxicity: Fetal harm may occur. Advise of potential risk and use effective contraception during treatment and 1 month following last dose.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

D69.3	Immune thrombocytopenic purpura

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the guideline creation.

DEFINITIONS:

Thrombocytopenic Purpura: any of various types associated with a decrease in the number of platelets in the blood; there are two general types: in the primary or idiopathic type, the cause is unknown. The secondary or symptomatic type may be associated with exposure to drugs or other chemical agents or with any of numerous different diseases. The most prominent symptoms are bruising and petechiae. In the acute form there may be bleeding from body orifices.

RELATED GUIDELINES:

Avatrombopag (Doptelet®), 09-J3000-02
Eltrombopag (Promacta®), 09-J1000-13
Immune Globulin Therapy, 09-J0000-06
Rituximab (Rituxan®), 09-J0000-59
Romiplostim Injection (Nplate™), 09-J0000-88

OTHER:

None applicable.

REFERENCES:

1. Clinical Pharmacology. [database online]. Tampa, FL: Gold Standard, Inc.; 2024. URL. www.Clinicalpharamcology-ip.com Accessed 11/30/24.
2. Micromedex ® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 11/30/24.
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(16):4190-4207.
4. Neunert C, Terrell DR, Arnold DM, et al. The American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019;3(23):3829-3866.

5. Newland A, Lee EJ, McDonald V, Bussel JB. Fostamatinib for persistent/chronic adult immune thrombocytopenia. *Immunotherapy* 2018;10(1):9-25.
6. Tavalisse (fostamatinib) [package insert]. Rigel Pharmaceuticals, Inc. South San Francisco, CA: Nov 2020.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/11/24.

GUIDELINE UPDATE INFORMATION:

06/15/18	New Medical Coverage Guideline.
09/15/19	Review and revision to guideline consisting of updating position statement and references.
12/15/19	Review and revision to guideline consisting of updating the position statement.
12/15/20	Review and revision to guideline consisting of updating the description and references.
12/15/21	Review and revision to guideline consisting of updating dosing and references.
12/15/22	Review and revision to guideline consisting of updating documentation of platelet improvement under continuation criteria and updating references.
12/15/23	Review and revision to guideline consisting of updating the position statement and references.
01/15/25	Review and revision to guideline consisting of updating the position statement for risk of bleeding.