fostamatinib (Tavalisse™)

Policy # 00638
Original Effective Date: 09/19/2018
Current Effective Date: 09/19/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider fostamatinib (Tavalisse™)‡ for the treatment of chronic immune thrombocytopenia to be **eligible for coverage.**

Patient Selection Criteria
Coverage eligibility for fostamatinib (Tavalisse) will be considered when the following criteria are met:

- The patient has a diagnosis of chronic immune thrombocytopenia (ITP); AND
- The patient is greater than or equal to 18 years of age; AND
- The patient has tried and failed (e.g. intolerance or inadequate response) at least ONE of the following alternative therapies: corticosteroids (e.g. dexamethasone, prednisone), intravenous immunoglobulin (IVIG), anti-D immunoglobulin, a thrombopoietin receptor agonist (e.g. eltrombopag [Promacta®]‡, romiplostim [Nplate®]‡), or rituximab (Rituxan®)‡.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of fostamatinib (Tavalisse) when patient selection criteria are not met to be **investigational.***

Background/Overview

Tavalisse is a tyrosine kinase inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment. The major metabolite of Tavalisse, R406, inhibits signal transduction by Fc-activating receptors and B-cell receptors to reduce the antibody-mediated destruction of platelets. Tavalisse should not be used in patients younger than 18 years of age because adverse events on actively growing bones were observed in nonclinical studies. Tavalisse should be initiated at a dose of 100 mg twice daily. If the platelet count does not increase to at least 50 $x10^9$/L after one month of therapy, the dose should be increased to 150 mg twice daily.

Chronic ITP is an acquired condition of thrombocytopenia in which autoantibodies destroy the platelets and also affect megakaryocytes and impair platelet production. ITP has previously been called idiopathic thrombocytopenic purpura, immune thrombocytopenic purpura, or autoimmune thrombocytopenic purpura, but these terms have been replaced by ITP to reflect the known immunologic mechanism and absence of

purpura in some patients. The 2011 American Society of Hematology (ASH) guidelines state that first-line treatment for adults with ITP includes corticosteroids or intravenous immunoglobulin (IVIG). For patients who are unresponsive or relapse after initial therapy, splenectomy is recommended. Thrombopoietin receptor agonists are recommended for patients with a bleeding risk who relapse following splenectomy, or have a contraindication to splenectomy and who have failed at least one other therapy. The guidelines also suggest that thrombopoietin receptor agonists be considered for those at risk of bleeding who have failed one line of therapy, such as corticosteroids or IVIG, and who have not undergone splenectomy. Rituximab is another second-line treatment option for patients who have failed corticosteroids or IVIG. The guidelines have not been updated to include Tavalisse. Of note, these guidelines only recommend treatment for newly-diagnosed adults with a platelet count <30 $x10^9$/L and do not recommend further treatment for asymptomatic patients after splenectomy who have achieved platelet counts >30 $x10^9$/L.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Tavalisse was approved in May 2018 for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Tavalisse was evaluated in two double-blind, placebo-controlled studies in a total of 150 patients with persistent or chronic ITP who had an insufficient response to previous treatment. In each study, patients were randomized 2:1 to Tavalisse or placebo for 24 weeks. Stable concurrent ITP therapy (glucocorticoids, azathioprine, or danazol) was allowed, and rescue therapy was permitted if needed. All patients initially received study drug at 100 mg twice daily (or matching placebo). Based on platelet count and tolerability, dose escalation to 150 mg twice daily (or matching placebo) was undertaken in 88% of patients at week 4 or later. Patients who did not respond to treatment after 12 weeks, as well as patients who completed the 24-week double blind study were eligible to enroll in an open-label extension study.

In both studies, the primary efficacy endpoint was stable platelet response which was defined as at least 50 $x10^9$/L on at least 4 of the 6 visits between weeks 14 to 24. In the first study (FIT-1), 18% of patients in the Tavalisse group achieved the primary endpoint compared to 0 in the placebo group (p=0.03). In the second study (FIT-2), 16% of patients in the Tavalisse group achieved the primary endpoint compared to 4% in the placebo group (not statistically significant).

References

1. Tavalisse [package insert]. Rigel Pharmaceuticals, Inc. South San Francisco, CA.

2. 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.

Policy History

Original Effective Date: 09/19/2018
Current Effective Date: 09/19/2018
09/06/2018 Medical Policy Committee review
09/19/2018 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 09/2019

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.