VENTURA COUNTY HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Thrombocytopenia – Tavalisse™ (fostamatinib disodium hexahydrate tablets – Rigel/Patheon Whitby)

DATE REVIEWED: 03/11/2020

OVERVIEW

Tavalisse, a tyrosine kinase inhibitor with demonstrated activity against spleen tyrosine kinase, is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.[1] The safety and efficacy of Tavalisse have not been established in pediatric patients. Use of Tavalisse is not recommended for patients < 18 years of age because adverse events on actively growing bones were observed in nonclinical studies. Discontinue Tavalisse if after 12 weeks of treatment the platelet count does not increase to a sufficient level to control bleeding.

Clinical Efficacy

The efficacy of Tavalisse was established in two identical, double-blind, placebo-controlled, multinational, randomized (2:1), 24-week studies (FIT-1 and FIT-2) in patients with persistent or chronic ITP with an insufficient response to previous therapies.[1,2] An open-label extension trial (FIT-3), involving patients from FIT-1 and FIT-2 was also performed.[1,3] In FIT-1 (n = 76), a stable platelet response (defined as at least 50 x 10^9/L on at least four of the six visits between Weeks 14 to 24) was achieved in 18% of patients (n = 9/51) who received Tavalisse compared with none of the patients who received placebo (P = 0.03).[1,2] In FIT-2 (n = 74), a stable platelet response was achieved in 16% of patients (n = 8/50) given Tavalisse vs. 4% of patients (n = 1/24) given placebo (a non statistically-significant difference). In FIT-1 and FIT-2, 47 patients given Tavalisse had received a prior thrombopoietin receptor agonist TPO-RA therapy, of which 17% of patients (n = 8/47) achieved a stable response. In FIT-3 (n = 123), 50% of the patients (n = 61/123) discontinued early. Of the 44 patients treated with placebo in the prior study, 23% of patients (n = 10/44) met the criteria for a stable response.

Guidelines

In 2019 the American Society of Hematology updated guidelines for immune thrombocytopenia.[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 (either Promacta® [eltrombopag tablets and oral suspension] or Nplate® [romiplostim injection for subcutaneous use]) 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 do not respond to first-line treatment, thrombopoietin receptor agonists are recommended. Other treatment options in children and adults include intravenous immunoglobulin (IVIG), anti-D immunoglobulin, and rituximab.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Tavalisse. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Tavalisse as well as the monitoring required for adverse event and long-term efficacy, approval requires Tavalisse to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tavalisse is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Chronic Immune Thrombocytopenia.** Approve for if the patient meets one of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets all of the following criteria (i, ii, iii, and iv):
     - **i.** The patient meets one of the following (a or b):
       - **a)** The patient has a platelet count < 30 x 10^9/L (< 30,000/µL): OR
       - **b)** The patient has a platelet count < 50 x 10^9/L (< 50,000/µL) and according to the prescriber the patient is at an increased risk of bleeding; AND
     - **ii.** The patient is ≥ 18 years of age; AND
     - **iii.** The agent is prescribed by or in consultation with a hematologist; AND
     - **iv.** The patient meets one of the following criteria (a or b):
       - **a)** The patient has tried at least one other therapy.
         Note: Examples of therapies are systemic corticosteroids, intravenous immunoglobulin, anti-D immunoglobulin, Promacta® (eltrombopag tablets and oral suspension), Nplate® (romiplostim injection for subcutaneous use), Doptelet® (avatrombopag tablets), or rituximab; OR
       - **b)** The patient has undergone splenectomy; OR
   - **B.** Continuation of Therapy. Approve for 1 year if the patient meets both of the following criteria (i and ii):
     - **i.** According to the prescriber the patient demonstrates a beneficial clinical response (e.g., increased platelet counts); AND
     - **ii.** The patient remains at risk for bleeding complications.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Tavalisse has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below.

1. **B-Cell Lymphomas.** Tavalisse has been investigated in patients with various B-cell lymphomas (e.g., non-Hodgkin's lymphoma, diffuse large B-cell lymphoma [DLBCL]).[5,6] Many other therapies are available for this use.

2. **Rheumatoid Arthritis.** Tavalisse has been studied in patients with rheumatoid arthritis.[7-11] However, other therapies are more well-established and are recommended in guidelines.

3. 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. Tavalisse™ tablets for oral use [prescribing information]. South San Francisco, CA and Whitby, Ontario: Rigel Pharmaceuticals and Patheon Whitby; April 2018.
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3. Bussel JB, Arnold DM, Boxer MA, et al. Long-term fostamatinib treatment of adults with immune thrombocytopenia during this phase 3 clinical trial program. *Am J Hematol*. 2019;94(5):546-553.
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.
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6. Friedberg JW, Sharman J, Sweetenham J, et al. Inhibition of Syk with fostamatinib disodium has significant clinical activity in non-Hodgkin lymphoma and chronic lymphocytic leukemia. *Blood*. 2010;115(13):2578-2585.
7. Genovese MC, van der Heijde DM, Keystone EC, et al. A phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study of 2 dosing regimens of fostamatinib in patients with rheumatoid arthritis with an inadequate response to a tumor necrosis factor-α antagonist. *J Rheumatol*. 2014;41(11):2120-2128.
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9. Weinblatt ME, Kavanaugh A, Genovese MC, et al. An oral spleen tyrosine kinase (SYK) inhibitor for rheumatoid arthritis. *N Engl J Med*. 2010;363(14):1303-1312.
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11. Kunwar S, Davkota AR, Ghimire DK. Fostamatinib, an oral spleen tyrosine kinase inhibitor, in the treatment of rheumatoid arthritis: a meta-analysis of randomized controlled trials. *Rheumatol Int*. 2016;36(8):1077-1087.