VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

TAC APPROVAL DATE: 07/03/2019

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.

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

The American Society of Hematology (ASH) has an evidence-based practice guideline for immune thrombocytopenia (2011).[4] This summary will focus on recommendations in adults, the population in which Tavalisse is indicated. Refer to the guideline for the management of younger patients or in specialized conditions (e.g., pregnancy). Treatment for adults is suggested for newly-diagnosed patients with a platelet count < 30 x 10^9/L. Therapies should be individualized and consider the bleeding severity, the desired time course for platelet increases, and AEs. For newly-diagnosed adults with ITP, longer courses of corticosteroids are preferred over shorter-courses of corticosteroids or IVIG as first-line therapy. When a more rapid increase in platelet count is required, intravenous immunoglobulin (IVIG) should be used with corticosteroids. If corticosteroids are contraindicated, either IVIG or anti-D immunoglobulin (in appropriate patients) may be used as first-line treatment. For the treatment of adults who do not respond or relapse following initial corticosteroids therapy, several strategies are employed. Splenectomy is recommended for patients who have failed corticosteroids. For patients at risk of bleeding who relapse following splenectomy or who have a contraindicated to splenectomy and have failed at least one other therapy, thrombopoietin receptor agonists can be given. Also, thrombopoietin receptor agonists may be considered for patients at risk of bleeding who have failed one line of therapy, such as corticosteroids or IVIG, and who have not undergone splenectomy. Rituximab may be an alternative for patients at risk of bleeding who have

failed one line of therapy (e.g., corticosteroids, IVIG, or splenectomy). No further treatment is recommended in asymptomatic patients after splenectomy who have achieved platelet counts > 30 x 10^9/L.

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 1 year if the patient meets the following criteria (A, B, and C):
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** The agent is prescribed by or in consultation with a hematologist; AND
   - **C)** The patient meets one of the following criteria (i or ii):
     - **i.** The patient has tried at least one other therapy. Note: Examples of therapies are corticosteroids, intravenous immunoglobulin, anti-D immunoglobulin, Promacta® (eltrombopag tablets and oral suspension), Nplate® (romiplostim injection for subcutaneous use), Doptelet® (avatrombopag tablets), or rituximab; OR
     - **ii.** The patient has undergone splenectomy.

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.

2. Bussel J, Arnold DM, Grossbard E, et al. Fostamatinib for the treatment of adult persistent and chronic immune thrombocytopenia: results of two phase 3, randomized, placebo-controlled trials. *Am J Hematol*. 2018;93(7):921-930.
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, 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.
5. Flinn IW, Bartlett NL, Blum KA, et al. A phase II trial to evaluate the efficacy of fostamatinib in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). *Eur J Cancer*. 2016;54:11-17.
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.
8. Weinblatt ME, Genovese MC, Ho M, et al. Effects of fostamatinib, an oral spleen tyrosine kinase inhibitor, in rheumatoid arthritis patients with an inadequate response to methotrexate: result from a phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. *Arthritis Rheumatol*. 2014;66(12):3255-3264.
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.
10. Taylor PC, Genovese MC, Greenwood M, et al. OSKIRA-4: a Phase IIb randomized, placebo-controlled study of the efficacy and safety of fostamatinib monotherapy. *Ann Rheumat Dis*. 2015;74(12):2123-2129.
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.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	--	05/02/2018
Annual revision	No criteria changes	05/22/2019
Early annual revision	The following criteria changes were made: 1. **Chronic Immune Thrombocytopenia:** Doptelet was added to the list of alternatives that count towards the criteria that requires a trial of at least one other therapy. Also, the approval duration was changed from 3 years to 1 year.	07/03/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committe.