Thrombopoietin Receptor Agonists and Tavalisse Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

Nplate is not a target in this program.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	08-01-2017

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Alvaiz ™ (eltrombopag) Tablet	• Treatment of thrombocytopenia in adult and pediatric patients 6 years and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Alvaiz should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. • Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. Alvaiz should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy • Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy Limitations of Use: • Alvaiz is not indicated for the treatment of patients with myelodysplastic syndrome (MDS) • Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection		16
Doptelet® (avatrombopag) Tablet	• Treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure • Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to previous treatment		1
Mulpleta® (lusutrombop	• Treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure		2

Agent(s)	FDA Indication(s)	Notes	Ref#
ag) Tablet			
Nplate® (romiplostim) Subcutaneous injection	• Treatment of thrombocytopenia in adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy • Treatment of thrombocytopenia in pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy • Increase survival in adults and in pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [HS-ARS]) Limitations of Use: • Nplate is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than ITP • Nplate should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding • Nplate should not be used in an attempt to normalize platelet counts		3
Promacta® (eltrombopag) Tablet Powder for oral suspension	• Treatment of thrombocytopenia in adult and pediatric patients 1 year and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding • Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. Promacta should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy • In combination with standard immunosuppressive therapy for the first-line treatment of adult and pediatric patients 2 years and older with severe aplastic anemia • Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy Limitations of Use: • Promacta is not indicated for the treatment of patients with myelodysplastic syndrome (MDS) • Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection		4

Agent(s)	FDA Indication(s)	Notes	Ref#
Tavalisse® (fostamatinib) Tablet	• Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment		5

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Immune (Idiopathic) Thrombocytopenia	Immune (idiopathic) thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by a low platelet count resulting from platelet destruction and impaired platelet production. ITP can be an isolated primary condition, or it may be secondary to other conditions. The goal of all treatment strategies for ITP is to achieve a platelet count that is associated with adequate hemostasis, rather than a normal platelet count. Bleeding events are often unpredictable and patients with ITP, even in the setting of severe thrombocytopenia, may not exhibit bleeding beyond bruising and petechiae. However, more serious mucosal bleeding may occur, including menorrhagia, epistaxis, gastrointestinal hemorrhage, hematuria, or, rarely, intra-cranial hemorrhage. The decision as to whether a patient can be observed or requires further intervention is highly complex and varies based on comorbidities, medications, and age, which all impact the risk of bleeding. In addition, management approaches may vary based on disease duration, access to care, quality-of-life implications, and patient and provider preferences, among other factors. An International Working Group consensus panel defines ITP as newly diagnosed (diagnosis to 3 months), persistent (3-12 months from diagnosis), or chronic (lasting for more than 12 months).(6) The American Society of Hematology (ASH) 2019 guidelines for immune thrombocytopenia separate treatments into adult and pediatric categories as well as initial vs secondary treatments in both groups. In adults with newly diagnosed ITP and a platelet count of less than 30 X 10^9/L who are asymptomatic or have minor mucocutaneous bleeding, ASH suggests corticosteroids rather than management with observation. There may be a subset of patients within this group for whom observation might be appropriate. This should include consideration of the severity of thrombocytopenia, additional comorbidities, use of anticoagulant or antiplatelet medications, need for upcoming procedures, and age of the patient.(6) In adults with newly diagnosed ITP and a platelet count greater than or equal to 30 X 10^9/L who are asymptomatic or have minor mucocutaneous bleeding, the ASH panel recommends against corticosteroids and in favor of management with observation. For patients with a platelet count at the lower end of this threshold, for those with additional comorbidities, anticoagulant or antiplatelet medications, or upcoming procedure, and for elderly (greater than 60 years old), treatment with corticosteroids may be appropriate.(6) In adult patients with ITP for greater than or equal to 3 months who are corticosteroid dependent or do not have a response to corticosteroids, the ASH panel suggests treatment with a thrombopoietin receptor agonist (the guidelines suggest either eltrombopag or romiplostim but also acknowledge no therapies available after 2017 were included in these guidelines), rituximab, or a splenectomy. The panel suggests use of a thrombopoietin receptor agonist over rituximab or a splenectomy and rituximab over a splenectomy. Each of these second-line treatments may be effective therapy and therefore the choice of treatment should be individualized based on duration of ITP, frequency of bleeding episodes requiring hospitalization or rescue

	medication, comorbidities, age of patient, medication adherence, medical and social support networks, patient values and preferences, cost, and availability.(6)
	
	In children with newly diagnosed ITP who have non-life-threatening mucosal bleeding and/or diminished health related quality of life (HRQoL), the panel suggests corticosteroids over IVIG or anti-D immunoglobulin but does suggest that IVIG or anti-D immunoglobulin could be used in certain situations.(6)
	
	In children with ITP who have non-life-threatening mucosal bleeding and/or diminished HRQoL and do not respond to first-line treatment the ASH panel suggests the use of thrombopoietin receptor agonists over rituximab or splenectomy and rituximab over splenectomy.(6)
	
	Given the impact of corticosteroids on mental health, the treating prescriber should assess HRQoL (e.g., depression, fatigue, mental status) while patients are receiving corticosteroids. Based on clinical experience, the ASH panel agreed there was likely trivial benefit in continuing corticosteroids in adults beyond 6 weeks. For the majority of patients, a trial of 6 weeks of corticosteroids should determine whether a patient is going to enter remission or will require additional therapy. For patients who require additional therapy, consideration of alternative therapy is preferred over ongoing exposure to corticosteroids. In children the ASH panel advises against courses of corticosteroids longer than 7 days.(6)
	
	Recommendations from the 2011 ASH guidelines that were not prioritized to be addressed, discussed or updated by the 2019 guideline panel were as follows:(6)
	
	• First-line treatment of adult ITP:
	  ○ IVIG with corticosteroids can be used when a more rapid increase in platelet count is required
	  ○ Either IVIG or anti-D (in appropriate patients) be used as a first-line treatment if corticosteroids are contraindicated

Chronic Hepatitis C associated thrombocytopenia(11)	A number of studies have suggested an association between hepatitis C virus (HCV) infection and immune thrombocytopenia (ITP) and/or autoimmune hemolytic anemia, either as a consequence of interferon therapy or in the setting of chronic infection without therapy. One of the largest studies included 120,691 United States veterans with chronic HCV who were matched with 454,905 controls. HCV was associated with ITP in both treated and untreated patients (hazard ratio 1.8).
Severe Aplastic Anemia	Aplastic Anemia is a diagnosis of exclusion. There is no single test that can be used to consistently diagnosis aplastic anemia from the multiple of other causes of bone marrow failure and the diagnostic evaluation must assess for and exclude these alterative etiologies. At initial presentation many patients exhibit fatigue, weakness, pallor, and headaches due to anemia. Often patients have petechiae of the skin and mucous membranes, epistaxis, and/or gum bleeding related to severe thrombocytopenia. Fever and infections can also be seen in these patients as a result of low white blood cell counts and neutropenia. Aplastic anemia patients identified earlier in the course of the disease by abnormalities found on routine laboratory testing may not have any physical manifestations of their disease.(15) Aplastic anemia is further classified clinically by the severity of the depression of the peripheral blood counts. Severe aplastic anemia is defined by a decrease in blood counts involving greater than or equal to 2 of the following hematopoietic lineages(15) • Absolute reticulocyte count less than 60 x 10^9/L • Absolute neutrophil count less than 0.5 X 10^9/L • Platelet count less than 20 x 10^9/L **AND**

	Bone marrow hypocellularity (less than 25% of the normal cellularity) Very severe aplastic anemia has an absolute neutrophil count less than 0.2 x 10^9/L and moderate aplastic anemia is characterized by the depression of blood counts not fulfilling the definition of severe disease.(15) The British Journal of Haematology guidelines for the diagnosis and management of adult aplastic anaemia define severe aplastic anemia as:(10) At least 2 of the following blood criteria: • Neutrophils less than 0.5 X 10^9/L • Platelets less than 20 X 10^9/L* • Reticulocytes less than 1% corrected (percentage of actual hematocrit [Hct] to normal Hct) or reticulocyte count less than 20 X 10^9/L **AND** 1 of the following marrow criteria: • Severe hypocellularity: less than 25% • Moderate hypocellularity, 25-50% with hematopoietic cells representing less than 30% of residual cells * Automated reticulocyte counting will over-estimate the count compared with the levels set in the Camitta criteria for defining disease severity, which were defined on manual counts. This criterion has now been modified from manual percentages to absolute reticulocyte levels less than 60 x 10^9/L as assessed by automated technologies.(10) The standard treatment for aplastic anemia is immunosuppressive therapy with horse antithymocyte globulin (ATG) and cyclosporine, and hematologic responses are observed in about two thirds of patients. Patients with disease that is refractory to immunosuppression and those who have a relapse after treatment may undergo allogeneic hematopoietic stem-cell transplantation (HSCT). However, 20 to 40% of patients without a suitable donor for HSCT continue to have severe cytopenias and are at risk for life-threatening hemorrhage due to thrombocytopenia and severe infections due to neutropenia. No standard therapies are available for patients who have aplastic anemia that is refractory to immunosuppression and are ineligible for HSCT, other than transfusions and treatment of infections. More than 40% of patients with disease that is refractory to immunosuppression die from bleeding or infection within 5 years after diagnosis. Although readministration of immunosuppressive therapy has been effective as salvage therapy in some patients, intensification of the regimen with more potent agents, such as rabbit ATG, sirolimus, or mycophenolate, has not improved the response rate.(8,9)
Thrombocytopenia in liver disease(12)	Patients with acute and chronic liver disease frequently acquire unique changes in hemodynamic and hemostatic pathways that may result in life-threatening bleeding and thrombosis. Additionally, activation of hemostatic pathways may play a role in disease progression through prechymal extinction, or organ atrophy, recruitment of inflammatory cells and activation of stellate cells. Traditional coagulation measures, including pro-thrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), and bleeding time (BT) do not measure bleeding risk in cirrhosis. In addition, platelet count alone provides an incomplete guide to bleeding risk in cirrhosis. However, values below 50,000/µL may be associated with a higher risk of bleeding. Procedure-related bleeding is common in cirrhosis patients but estimates of incidence vary widely. For many years, the PT/INR served as a surrogate marker for estimating

	bleeding risk in cirrhosis. However, use of INR and arbitrary "cut-offs" as a clinical target is not recommended or supported by scientific evidence. Assessment of individual patient characteristics is also essential as clinical factors, such as acute kidney injury or infection may alter bleeding risk in certain clinical scenarios. In elective and planned settings, such as planned dental extractions or other invasive procedures with moderate or high risk, thrombopoietin receptor agonists are an alternative means to increase platelets prior to invasive procedures.

Hematopoietic syndrome of acute radiation syndrome	Acute radiation syndrome (ARS) (sometimes known as radiation toxicity or radiation sickness) refers to a spectrum of pathophysiological effects that are induced when high doses of ionizing radiation interact with the human body.(13) The major cause of this syndrome is depletion of immature parenchymal stem cells in specific tissues. The required conditions for ARS are:(14)
	
	• The radiation dose must be large (i.e., greater than 0.7 Gray (Gy) or 70 rads)
	  ○ Mild symptoms may be observed with doses as low as 0.3 Gy or 30 rads
	• The dose usually must be external (i.e., the source of radiation is outside of the patient's body)
	  ○ Radioactive materials deposited inside the body have produced some ARS effects only in extremely rare cases
	• The radiation must be penetrating (i.e., able to reach internal organs)
	  ○ High energy X-rays, gamma rays, and neutrons are penetrating radiations
	• The entire body (or a significant portion of it) must have received the dose
	  ○ Most radiation injuries are local, frequently involving the hands, and these local injuries seldom cause classical signs of ARS
	• The dose must have been delivered in a short time (usually a matter of minutes)
	  ○ Fractionated doses are often used in radiation therapy. These are large total doses delivered in small daily amounts over a period of time. Fractionated doses are less effective at inducing ARS than a single dose of the same magnitude
	
	The four classic ARS syndromes are hematopoietic syndrome, gastrointestinal (GI) syndrome, cardiovascular (CV) syndrome, and central nervous system (CNS) syndrome. Of the 4, the hematopoietic syndrome is the only one that may be reversed through medical intervention.(13)
	
	The full syndrome of hematopoietic syndrome will usually occur with a dose between 0.7 and 10 Gy (70-1000 rads) though mild symptoms may occur as low as 0.3 Gy or 30 rads. The survival rate of patient with bone marrow syndrome decreases with increasing dose. The primary cause of death is the destruction of the bone marrow resulting in infection and hemorrhage.(14)

Efficacy	**Doptelet(1)** Doptelet (avatrombopag) is a thrombopoietin receptor agonist that stimulates proliferation and differentiation of megakaryocytes from bone marrow progenitor cells resulting in an increased production of platelets. The efficacy of Doptelet for the treatment of thrombocytopenia in patients with chronic liver disease who are scheduled to undergo a procedure was established in 2 identically-designed multicenter, randomized, double-blind, placebo-controlled trials (ADAPT-1 and ADAPT-2). In each study, patients were assigned to the low baseline platelet count cohort (less than 40 X 10^9/L) or high baseline platelet count cohort (greater than or equal to 40 to less than 50 X 10^9/L) based on their platelet count at baseline. In the ADAPT-1 trial 149 patients were treated with Doptelet and 82 patients were treated with placebo both once daily for 5 days. In the ADAPT-2 trial, 128 patients were treated with Doptelet and 76 patients were treated with placebo. Across both

	baseline platelet count cohorts and the Doptelet and placebo treatment groups, patients underwent a broad spectrum of types of scheduled procedures that ranged from low to high bleeding risk. The major efficacy outcome in both trials was the proportion of patients who did not require a platelet transfusion or any rescue procedure for bleeding after randomization and up to 7 days following an elective procedure. Additional secondary efficacy outcomes were the proportion of patients who achieved platelet counts of greater than or equal to 50 X 10^9/L on the day of procedure and the change in platelet count from baseline to procedure day. Responders were defined as patients who did not require a platelet transfusion or any rescue procedure (whole blood transfusion, packed red blood cell transfusion, platelet transfusion, fresh frozen plasma or cryoprecipitate administration, Vitamin K, desmopressin, recombinant activated factor VII, aminocaproic acid, tranexamic acid, or surgical or interventional radiology performed to achieve hemostasis and control blood loss) for bleeding after randomization and up to 7 days following a scheduled procedure. In both baseline platelet count cohorts, patients in the Doptelet treatment groups had a greater proportion of responders than the corresponding placebo treatment groups that was both clinically meaningful and statistically significant. The percentage of responders in the low baseline platelet count cohort and treatment group that responded in the ADAPT-1 trial was 66% in the Doptelet group and 23% in the placebo group (p-value less than 0.0001). In the Adapt-2 trial the percentage of responders was 69% in the Doptelet group and 35% in the placebo group (p-value 0.0006). The percentage of responders in the high baseline platelet count cohort in ADAPT-1 trial was 88% in the Doptelet group and 38% in the placebo group (p-value less than 0.0001). In the ADAPT-2 trial the percentage of responders was 88% in the Doptelet group and 33% in the placebo group (p-value less than 0.0001). Both trials also demonstrated a higher proportion of patients who achieved the target platelet count of greater than or equal to 50 X 10^9/L on the day of the procedure (a secondary efficacy endpoint) and a greater mean change in platelet counts from baseline to the day of the procedure (a secondary efficacy endpoint). The efficacy of Doptelet in adult patients with chronic immune thrombocytopenia was evaluated in a phase 3, multicenter, randomized, double-blind, placebo-controlled trial (NCT01438840). Patients had received one or more chronic immune thrombocytopenia therapies and had an average platelet count of 30 X 10^9/L. The major efficacy outcome was the cumulative number of weeks in which the platelet count was greater than or equal to 50 X 10^9/L during the 6-month treatment period in the 6-month treatment period in the absence of rescue therapy. Doptelet-treated patients had a longer duration of platelet counts greater than or equal to 50 x10^9/L in the absence of rescue therapy than those who received placebo (median 12.4 [0, 25] vs 0 [0, 2] weeks, respectively, p less than 0.0001. In addition, a larger proportion of patients in the Doptelet treatment group had platelet counts greater than or equal to 50 X 10^9/L at Day 8 compared to placebo (21/32; 66% vs 0/17; 0.0%, respectively; p less than 0.0001). **Mulpleta(2)** Mulpleta (lusutrombopag) is an orally bioavailable TPO receptor agonist that interacts with the transmembrane domain of human TPO receptors expressed on megakaryocytes to induce the proliferation and differentiation of megakaryocytic progenitor cells from hematopoietic stem cells and megakaryocyte maturation. The efficacy of Mulpleta for the treatment of thrombocytopenia in patients with chronic liver disease who are scheduled to undergo a procedure was evaluated in 2 randomized, double-blind, placebo-controlled trial (L-PLUS 1 and L-PLUS 2). Patients

	with chronic liver disease who were undergoing an invasive procedure and had a platelet count less than 50 X 10^9/L were eligible to participate. Patients were randomized to receive 3 mg of Mulpleta or placebo once daily for up to 7 days. In L-PLUS 1 the major efficacy outcome was the proportion of patients who require no platelet transfusion prior to the primary invasive procedure. In L-PLUS 2 the major efficacy outcome was the proportion of patients who required no platelet transfusion prior to the primary invasive procedure and no rescue therapy for bleeding (i.e., platelet preparations, other blood preparations, including red blood cells and plasma, volume expanders) from randomization through 7 days after the primary invasive procedure. In both the L-PLUS 1 and L-PLUS 2 trials, responders were defined as patients who had a platelet count of greater than or equal to 50 X 10^9/L with an increase of greater than or equal to 20 X 10^9/L from baseline. In the L-PLUS 1 trial the percentage of patients not requiring platelet transfusion prior to invasive procedure was 78% in the Mulpleta arm and 13% in the placebo arm (95% CI, p-value less than 0.0001). The percentage of patients that responded during the study was 76% in the Mulpleta arm and 6% in the placebo arm (95%CI, p-value less than 0.001). In the L-Plus 2 trial the percentage of patients not requiring platelet transfusion prior to invasive procedure or rescue therapy for bleeding from randomization through 7 days after invasive procedure was 65% in the Mulpleta arm and 29% in the placebo arm (95% CI, p-value less than 0.0001). The percentage of patients that responded during the study was 65% in the Mulpleta arm and 13% in the placebo arm (95%CI, p-value less than 0.001). **Nplate(3)** Nplate (romiplostim) is a thrombopoietin receptor agonist that increases platelet production through binding and activation of the thrombopoietin (TPO) receptor, similar in mechanism to endogenous TPO. The safety and efficacy of Nplate were assessed in two double-blind, placebo-controlled clinical studies, in an open-label single-arm study, and in an open-label extension study. Efficacy in all studies was defined as maintaining a target platelet count greater than or equal to 50 X 10^9/L. The safety and efficacy of Nplate in pediatric patients 1 year and older with ITP for at least 6 months were assessed in two double-blind, placebo controlled clinical trials. The efficacy in both studies was defined as maintaining a target platelet count of greater than or equal to 50 X 10^9/L. Efficacy studies of Nplate could not be conducted in humans with acute radiation syndrome for ethical and feasibility reasons. Approval for this indication was based on efficacy studies conducted in animals, Nplate's effect on platelet count in healthy human volunteers, and on data supporting Nplate's effect on thrombocytopenia in patients with ITP and insufficient response to corticosteroids, immunoglobulins, or splenectomy. **Promacta(4)** Promacta (eltrombopag) interacts with the transmembrane domain of the TPO receptor (also known as cMpl) leading to increased platelet production. Safety and efficacy of Promacta in adult patient with persistent or chronic ITP were evaluated in three randomized, double-blind, placebo-controlled trials and in an open-label extension trial. Safety and efficacy of Promacta in pediatric patients 1 year and

	older with chronic ITP were evaluated in two double-blind, placebo-controlled trials. All of these trials showed clinically significant efficacy of Promacta vs placebo. Safety and efficacy of Promacta was evaluated in 2 randomized, double-blind, placebo-controlled trials for eltrombopag in treating thrombocytopenia in patients with chronic hepatitis C. One trial used peginterferon alfa-2a (Pegasys); the other used peginterferon alfa-2b (Pegintron), both were in combination with ribavirin. Approximately 30% of patients had been previously treated with interferon and ribavirin. Patients had to have platelet counts of less than 75 x10^9/L. The trials consisted of 2 phases: a pre-antiviral treatment phase and an antiviral treatment phase. Patients were allowed to be randomized for the antiviral treatment phase if they reached the platelet count threshold of greater than or equal to 90 X 10^9/L (trial 1) and greater than or equal to 100 x 10^9/L (trial 2). The maximum allowed time on open label eltrombopag was 9 weeks. The primary efficacy endpoint for both studies was sustained virologic response (SVR) defined as the percentage of patients with undetectable HCV-RNA at 24 weeks after completion of antiviral treatment. The median time to achieve the target platelet count in study 1 was approximately 2 weeks with 95% of patients initiating antiviral therapy. The safety of Promacta as first-line treatment of severe aplastic anemia was established based on a single-arm trial of 153 patients with severe aplastic anemia who had not received prior definitive immunosuppressive therapy. In this trial, Promacta was administered in combination with horse antithymocyte globulin (h-ATG) and cyclosporine. The efficacy of Promacta in combination with h-ATG and cyclosporine was established on the basis of complete hematological response at 6 months. A complete response was defined as hematological parameters meeting all 3 of the following values on 2 consecutive serial blood count measurements at least one week apart: absolute neutrophil count (ANC) greater than 1,000/microliter, platelet count greater than 100 X 10^9/L, and hemoglobin greater than 10 g/dL. A partial response was defined as blood counts no longer meeting the standard criteria for severe pancytopenia in severe aplastic anemia equivalent to 2 of the following values on 2 consecutive serial blood count measurements at least one week apart: ANC greater than 500/microliter, platelet count greater than 20 X 10^9/L, or reticulocyte count greater than 60,000/microliter. Overall response rate is defined as the number of partial responses plus complete responses. The overall response rate at month 6 was 79% (95% CI). The median duration of overall response was 70 months (95% CI). The median duration of complete response was 46 months (95% CI). Promacta was studied in a single-arm, single-center, open-label trial in 43 patients with severe aplastic anemia who had an insufficient response to at least one prior immunosuppressive therapy and who had a platelet count of less than or equal to 30 X 10^9/L. The efficacy was evaluated by the hematologic response assessed after 12 weeks of treatment. Hematologic response was defined as meeting 1 or more of the following criteria: 1) platelet count increases to 20 X 10^9/L above baseline, or stable platelet counts with transfusion independence for a minimum of 8 weeks; 2) hemoglobin increase by greater than 1.5 g/dL, or a reduction in greater than or equal to 4 units of red blood cell transfusions for 8 consecutive weeks; 3) ANC increase of 100% or an ANC increase greater than 0.5 X 10^9/L Promacta was discontinued after 16 weeks if no hematologic response was observed. The response rate was 40% (95% CI) and the median of duration of response was not reached due to few events. **Tavalisse(5)** Tavalisse (fostamatinib) is a tyrosine kinase inhibitor with demonstrated activity against spleen tyrosine kinase. Tavalisse was studied in two placebo-controlled efficacy and safety studies (FIT-1 and FIT-2), and an open-label extension study (FIT-3). A total of 150 patients with persistent or chronic immune thrombocytopenia, who had an insufficient response to previous treatment (which included corticosteroids,

	immunoglobulins, splenectomy, and/or a thrombopoietin receptor agonists) were enrolled in two identical, double-blind, placebo-controlled studies that were conducted in different countries. For each study, patients were randomized to receive Tavalisse or placebo for 24 weeks. 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 the open-label extension study. The efficacy of Tavalisse was based on stable platelet response (at least 50 X 10^9/L on at least 4 of the 6 visits between weeks 14 to 24). The percent of patients who had a stable platelet response was 16-18% in the Tavalisse arms and 0-1% in the placebo arms. The FIT-3 extension study enrolled 123 patients who completed 24 weeks of treatment in the FIT-1 and FIT-2 studies, or who did not respond to treatment any time after 12 weeks in these studies. Patients who were designated as responders in the FIT-1 and FIT-2 studies (defined as platelet count of at least 50 X 10^9/L) at the time of rollover continued in the extension study at their current trial dose and regimen. Patients who entered the extension study as non-responders (defined as platelet count less than 50 X 10^9/L) received Tavalisse 100 mg twice daily regardless of their dose and regimen in the prior study. Stable response in this study was prospectively defined as no 2 visits, at least 4 weeks apart, with a platelet count less than 50 X 10^9/L, without an intervening visit with a platelet count of at least 50 X 10^9/L (unrelated to rescue therapy), within a period of 12 weeks following initial achievement of the target platelet count. Among the patients who achieved stable response in FIT-1, FIT-2, and FIT-3 trials, 18 patients maintained the platelet count of at least 50 X 10^9/L for 12 months or longer.
Safety(1-5)	All of the targeted agents have no FDA labeled contraindications.

REFERENCES

Number	Reference
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2	Mulpleta prescribing information. Shionogi Inc. April 2020.
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4	Promacta prescribing information. Novartis. March 2023.
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15	DeZern, A. E., & Churpek, J. E. (2021). Approach to the diagnosis of aplastic anemia. Blood Advances, 5(12), 2660–2671. https://doi.org/10.1182/bloodadvances.2021004345
16	Alvaiz prescribing information. Teva Pharmaceuticals, Inc. February 2024.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Doptelet	avatrombopag maleate tab	20 MG	M ; N ; O ; Y	N		
Alvaiz	eltrombopag choline tab	18 MG ; 36 MG ; 54 MG ; 9 MG	M ; N ; O ; Y	N		
Promacta	eltrombopag olamine powder pack for susp ; eltrombopag olamine tab	12.5 MG ; 25 MG ; 50 MG ; 75 MG	M ; N ; O ; Y	N		
Tavalisse	fostamatinib disodium tab	100 MG ; 150 MG	M ; N ; O ; Y	N		
Mulpleta	lusutrombopag tab	3 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Alvaiz	eltrombopag choline tab	9 MG	30	Tablets	30	DAYS			
Alvaiz	eltrombopag choline tab	18 MG	30	Tablets	30	DAYS			
Alvaiz	eltrombopag choline tab	36 MG	60	Tablets	30	DAYS			
Alvaiz	eltrombopag choline tab	54 MG	60	Tablets	30	DAYS			
Doptelet	Avatrombopag Maleate Tab 20 MG (Base Equiv)	20 MG	60	Tablets	30	DAYS			
Mulpleta	Lusutrombopag Tab 3 MG	3 MG	7	Tablets	7	DAYS			
Promacta	Eltrombopag Olamine Powder Pack for Susp 12.5 MG (Base Eq)	12.5 MG	30	Packets	30	DAYS			
Promacta	Eltrombopag Olamine Powder Pack	25 MG	30	Packets	30	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
	for Susp 25 MG (Base Equiv)								
Promacta	Eltrombopag Olamine Tab 12.5 MG (Base Equiv)	12.5 MG	30	Tablets	30	DAYS			
Promacta	Eltrombopag Olamine Tab 25 MG (Base Equiv)	25 MG	30	Tablets	30	DAYS			
Promacta	Eltrombopag Olamine Tab 50 MG (Base Equiv)	50 MG	60	Tablets	30	DAYS			
Promacta	Eltrombopag Olamine Tab 75 MG (Base Equiv)	75 MG	60	Tablets	30	DAYS			
Tavalisse	fostamatinib disodium tab	100 MG ; 150 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Alvaiz	eltrombopag choline tab	18 MG ; 36 MG ; 54 MG ; 9 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Doptelet	avatrombopag maleate tab	20 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Mulpleta	lusutrombopag tab	3 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Promacta	eltrombopag olamine powder pack for susp ; eltrombopag olamine tab	12.5 MG ; 25 MG ; 50 MG ; 75 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Tavalisse	fostamatinib disodium tab	100 MG ; 150 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Alvaiz	eltrombopag choline tab	54 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Alvaiz	eltrombopag choline tab	36 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Alvaiz	eltrombopag choline tab	18 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Alvaiz	eltrombopag choline tab	9 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Doptelet	Avatrombopag Maleate Tab 20 MG (Base Equiv)	20 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Mulpleta	Lusutrombopag Tab 3 MG	3 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Promacta	Eltrombopag Olamine Powder Pack for Susp 12.5 MG (Base Eq)	12.5 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Promacta	Eltrombopag Olamine Powder Pack for Susp 25 MG (Base Equiv)	25 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Promacta	Eltrombopag Olamine Tab 12.5 MG (Base Equiv)	12.5 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Promacta	Eltrombopag Olamine Tab 25 MG (Base Equiv)	25 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Promacta	Eltrombopag Olamine Tab 50 MG (Base Equiv)	50 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Promacta	Eltrombopag Olamine Tab 75 MG (Base Equiv)	75 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Tavalisse	fostamatinib disodium tab	100 MG ; 150 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when the ALL of the following are met: 1. ONE of the following: A. The requested agent is Doptelet AND ONE of the following: 1. The patient has a diagnosis of chronic (defined as lasting for at least 12 months) immune (idiopathic) thrombocytopenia (ITP) AND BOTH of the following: A. ONE of the following: 1. The patient has a platelet count less than or equal to 30 X 10^9/L **OR** 2. The patient has a platelet count greater than 30 X 10^9/L but less than 50 X 10^9/L AND has symptomatic bleeding and/or an increased risk for bleeding **AND** B. ONE of the following: 1. The patient has tried and had an inadequate response to ONE corticosteroid used for the treatment of ITP **OR** 2. The patient has an intolerance or hypersensitivity to ONE corticosteroid used for the treatment of ITP **OR** 3. The patient has an FDA labeled contraindication to ALL corticosteroids used for the treatment of ITP **OR** 4. The patient has tried and had an inadequate response to another thrombopoietin receptor agonist (e.g., Nplate, Promacta) or Tavalisse **OR** 5. The patient has tried and had an inadequate response to immunoglobulins (IVIg or Anti-D) **OR** 6. The patient has had an inadequate response to a splenectomy **OR** 7. The patient has tried and had an inadequate response to rituximab **OR** 8. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 9. The prescriber has provided documentation that corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** 2. The patient has a diagnosis of thrombocytopenia and has chronic liver disease AND ALL of the following: A. The patient has a platelet count less than 50 X 10^9/L **AND** B. The patient is scheduled to undergo a procedure with an associated risk of bleeding (e.g., gastrointestinal endoscopy, liver biopsy, bronchoscopy, dental procedure) **AND** C. The patient would require a platelet transfusion unless platelet counts are clinically increased from baseline (prior to therapy with the requested agent) **OR** 3. The patient has another FDA approved indication for the requested agent **OR**

Module	Clinical Criteria for Approval
	4. The patient has another indication supported in compendia for the requested agent **OR** B. The requested agent is Mulpleta (lusutrombopag) AND ONE of the following: 1. BOTH of the following: A. The patient has a platelet count less than 50 X 10^9/L **AND** B. The patient has a diagnosis of thrombocytopenia and has chronic liver disease AND BOTH of the following: 1. The patient is scheduled to undergo a procedure with an associated risk of bleeding (e.g., gastrointestinal endoscopy, liver biopsy, bronchoscopy, dental procedure) **AND** 2. The patient would require a platelet transfusion unless platelet counts are clinically increased from baseline (prior to therapy with the requested agent) **OR** 2. The patient has another FDA approved indication for the requested agent **OR** 3. The patient has another indication supported in compendia for the requested agent **OR** C. The requested agent is Nplate (romiplostim) AND ONE of the following: 1. The patient has a diagnosis of hematopoietic syndrome of acute radiation syndrome (HS-ARS) **OR** 2. The patient has a diagnosis of immune (idiopathic) thrombocytopenia (ITP) AND ALL of the following: A. ONE of the following: 1. The patient is between the ages of 1 and 17 years old AND the diagnosis has lasted for at least 6 months **OR** 2. The patient is 18 years old or over **AND** B. ONE of the following: 1. The patient has a platelet count less than or equal to 30 X 10^9/L **OR** 2. The patient has a platelet count greater than 30 X 10^9/L but less than 50 x 10^9/L AND has symptomatic bleeding and/or an increased risk for bleeding **AND** C. ONE of the following: 1. The patient has tried and had an inadequate response to ONE corticosteroid used for the treatment of ITP **OR** 2. The patient has an intolerance or hypersensitivity to ONE corticosteroid used for the treatment of ITP **OR** 3. The patient has an FDA labeled contraindication to ALL corticosteroids used for the treatment of ITP **OR** 4. The patient has tried and had an inadequate response to immunoglobulins (IVIg or anti-D) **OR** 5. The patient has had an inadequate response to a splenectomy **OR** 6. The patient has tried and had an inadequate response to rituximab **OR** 7. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 8. The prescriber has provided documentation that corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR**

Module	Clinical Criteria for Approval
	3. The patient has another FDA approved indication for the requested agent **OR** 4. The patient has another indication supported in compendia for the requested agent **OR** D. The requested agent is Promacta (eltrombopag) or Alvaiz AND ONE of the following: 1. The patient has a diagnosis of hepatitis C associated thrombocytopenia AND ONE of the following: A. The intent of therapy with the requested agent is to increase platelet counts sufficiently to initiate pegylated interferon therapy AND the patient's platelet count is less than 75 x 10^9/L **OR** B. The patient is on concurrent therapy with a pegylated interferon and ribavirin AND is at risk for discontinuing hepatitis C therapy due to thrombocytopenia **OR** 2. The patient has a diagnosis of severe aplastic anemia AND ALL of the following: A. The patient has at least 2 of the following blood criteria: 1. Neutrophils less than 0.5 X 10^9/L 2. Platelets less than 30 X 10^9/L 3. Reticulocyte count less than 60 X 10^9/L **AND** B. The patient has 1 of the following marrow criteria: 1. Severe hypocellularity: less than 25% **OR** 2. Moderate hypocellularity, 25-50% with hematopoietic cells representing less than 30% of residual cells **AND** C. ONE of the following: 1. BOTH of the following: A. The patient will use the requested agent as first-line treatment **AND** B. The patient will use the requested agent in combination with standard immunosuppressive therapy (i.e., antithymocyte globulin [ATG] AND cyclosporine) **OR** 2. ONE of the following: A. The patient has tried and had an inadequate response to BOTH antithymocyte globulin (ATG) AND cyclosporine therapy **OR** B. The patient has an intolerance or hypersensitivity to BOTH ATG AND cyclosporine **OR** C. The patient has an FDA labeled contraindication to BOTH ATG AND cyclosporine **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that BOTH antithymocyte globulin (ATG) AND cyclosporine therapy cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR**

Module	Clinical Criteria for Approval
	3. The patient has a diagnosis of persistent or chronic (defined as lasting for at least 3 months) immune (idiopathic) thrombocytopenia (ITP) AND BOTH of the following: A. ONE of the following: 1. The patient has a platelet count less than or equal to 30 x 10^9/L **OR** 2. The patient has a platelet count greater than 30 x 10^9/L but less than 50 x 10^9/L AND has symptomatic bleeding and/or an increased risk for bleeding **AND** B. ONE of the following: 1. The patient has tried and had an inadequate response to ONE corticosteroid used for the treatment of ITP **OR** 2. The patient has an intolerance or hypersensitivity to ONE corticosteroid used for the treatment of ITP **OR** 3. The patient has an FDA labeled contraindication to ALL corticosteroids used for the treatment of ITP **OR** 4. The patient has tried and had an inadequate response to immunoglobulins (IVIg or anti-D) **OR** 5. The patient has had an inadequate response to a splenectomy **OR** 6. The patient has tried and had an inadequate response to rituximab **OR** 7. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 8. The prescriber has provided documentation that corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** 4. The patient has another FDA approved indication for the requested agent **OR** 5. The patient has another indication supported in compendia for the requested agent **OR** E. The requested agent is Tavalisse (fostamatinib disodium hexahydrate) AND ONE of the following: 1. The patient has a diagnosis of chronic (defined as lasting for at least 12 months) immune (idiopathic) thrombocytopenia (ITP) AND BOTH of the following: A. ONE of the following; 1. The patient has a platelet count less than or equal to 30 X 10^9/L **OR** 2. The patient has a platelet count greater than 30 X 10^9/L but less than 50 x 10^9/L AND has symptomatic bleeding and/or an increased risk for bleeding **AND** B. ONE of the following: 1. The patient has tried and had an inadequate response to ONE corticosteroid used for the treatment of ITP **OR** 2. The patient has an intolerance or hypersensitivity to ONE corticosteroid used for the treatment of ITP **OR** 3. The patient has an FDA labeled contraindication to ALL corticosteroids used for the treatment of ITP **OR**

Module	Clinical Criteria for Approval
	4. The patient has tried and had an inadequate response to a thrombopoietin receptor agonist (e.g., Doptelet, Nplate, Promacta) **OR** 5. The patient has tried and had an inadequate response to immunoglobulins (IVIg or Anti-D) **OR** 6. The patient has had an inadequate response to a splenectomy **OR** 7. The patient has tried and had an inadequate response to rituximab **OR** 8. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 9. The prescriber has provided documentation that corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** 2. The patient has another FDA approved indication for the requested agent **OR** 3. The patient has another indication supported in compendia for the requested agent **AND** 2. If the patient has an FDA approved indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. ONE of the following: A. The patient will NOT use the requested agent in combination with another agent included in this program **OR** B. The patient will use the requested agent in combination with another agent included in this program AND BOTH of the following: 1. The requested agent is Nplate **AND** 2. The patient has a diagnosis of hematopoietic syndrome of acute radiation syndrome (HS-ARS) **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence NCCN 1 or 2a recommended use **Lengths of Approval:** **Doptelet:** thrombocytopenia in patients with chronic liver disease who are scheduled to undergo a procedure - 1 month; all other indications - 6 months **Mulpleta:** thrombocytopenia in patients with chronic liver disease who are scheduled to undergo a procedure - 1 month; all other indications - 6 months **Nplate:** HS-ARS - 1 time; ITP - 4 months; all other indications - 6 months **Promacta:** ITP - 2 months; thrombocytopenia in hep C - 3 months; first-line therapy in severe aplastic anemia - 6 months; all other severe aplastic anemia - 4 months; all other indications - 6 months **Alvaiz:** ITP - 2 months; thrombocytopenia in hep C - 3 months; all other severe aplastic anemia - 4 months; all other indications - 6 months **Tavalisse:** all indications - 6 months

Module	Clinical Criteria for Approval
	NOTE if Quantity Limit applies, please see Quantity Limit criteria **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process. Note: Doptelet and Mulpleta for thrombocytopenia with chronic liver disease AND Nplate for hematopoietic syndrome of acute radiation syndrome (HS-ARS) should always be reviewed under initial criteria **AND** 2. ONE of the following: A. The patient has a diagnosis of immune (idiopathic) thrombocytopenia (ITP) AND ONE of the following: 1. The patient's platelet count is greater than or equal to 50 x 10^9/L **OR** 2. The patient's platelet count has increased sufficiently to avoid clinically significant bleeding **OR** B. The patient has the diagnosis of hepatitis C associated thrombocytopenia AND BOTH of the following: 1. ONE of the following: A. The patient will be initiating hepatitis C therapy with pegylated interferon and ribavirin **OR** B. The patient will be maintaining hepatitis C therapy with pegylated interferon and ribavirin **AND** 2. ONE of the following: A. The patient's platelet count is greater than or equal to 90 x 10^9/L **OR** B. The patient's platelet count has increased sufficiently to initiate or maintain pegylated interferon based therapy for the treatment of hepatitis C **OR** C. The patient has another indication for the requested agent AND has shown clinical improvement (i.e., decreased symptom severity and/or frequency) **AND** 3. The patient will NOT use the requested agent in combination with another agent included in this program **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Lengths of Approval:** thrombocytopenia in hepatitis C - 6 months; all other indications - 12 months NOTE if Quantity Limit Applies, please see Quantity Limit criteria

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND**

Module	Clinical Criteria for Approval
	C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Initial Lengths of Approval:** **Doptelet:** thrombocytopenia in patients with chronic liver disease who are scheduled to undergo a procedure - 1 month; all other indications - up to 6 months **Mulpleta:** thrombocytopenia in patients with chronic liver disease who are scheduled to undergo a procedure - 1 month; all other indications - up to 6 months **Nplate:** HS-ARS - 1 time; ITP - up to 4 months; all other indications - up to 6 months **Promacta:** ITP - up to 2 months; thrombocytopenia in hep C - up to 3 months; first-line therapy in severe aplastic anemia - up to 6 months; all other severe aplastic anemia - up to 4 months; all other indications - up to 6 months **Alvaiz:** ITP - 2 months; thrombocytopenia in hep C - 3 months; all other severe aplastic anemia - 4 months; all other indications - 6 months **Tavalisse:** all indications - up to 6 months **Renewal Lengths of Approval:** thrombocytopenia in hepatitis C - up to 6 months; all other indications - up to 12 months