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Subject: Thrombocytopenia Oral Therapy

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DESCRIPTION:

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 FDA has approved the following oral therapies for the treatment of chronic ITP: avatrombopag (Doptelet, Doptelet Sprinkle), eltrombopag (Promacta, Alvaiz), fostamatinib (Tavalisse), and rilzabrutinib (Wayrilz). Avatrombopag (Doptelet, Doptelet Sprinkle), and Lusutrombopag (Mulpleta) are also FDA approved for the treatment of thrombocytopenia in adults with chronic liver disease (CLD) who are scheduled to undergo a procedure. Eltrombopag (Promacta, Alvaiz) is also FDA approved for the treatment of thrombocytopenia in persons with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy, for patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy, and for the initial treatment of severe aplastic anemia in combination with standard immunosuppressive therapy (antithymocyte globulin and cyclosporine). The NCCN guidelines provide recommendations for the use of eltrombopag to treat

chemotherapy-induced thrombocytopenia, immune-checkpoint inhibitor and immune-effector cell induced thrombocytopenia, and low risk myelodysplastic syndromes.

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 the requested agent **meets the definition of medical necessity** when used to for the treatment of **ONE** of the following conditions in Table 1 and **ALL** of the associated criteria are met:.

Table 1. Oral therapy for thrombocytopenia	
Avatrombopag (Doptelet, Doptelet Sprinkle),	**ONE** of the following: A. Chronic liver disease (CLD) and **ALL** of the following are met: 1. The member's platelet count is less than 50 x10^9/L - lab documentation must be submitted 2. The member is scheduled to undergo an elective procedure with an associated risk of bleeding that would require a platelet transfusion 3. The elective procedure is scheduled to occur 10 to 13 days after initiation of therapy with avatrombopag 4. The member does not have a history of thrombosis or a genetic prothrombotic condition (e.g., Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency, or Protein C or S deficiency) 5. Avatrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Alvaiz, Promacta], lusutrombopag [Mulpleta]) 6. The dosage does not exceed the following and will be achieved using the fewest number of tablets per day: a. Platelet count less than 40 x10^9/L: 60 mg tablet once daily for 5 days

	b. Platelet count greater than or equal to 40 x10^9/L to less than 50 x10^9/L: 40 mg tablet once daily for 5 days B. Chronic immune (idiopathic) thrombocytopenic purpura (ITP) and **ALL** of the following are met: 1. The member has demonstrated an insufficient response to **EITHER** 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]) 2. **ONE** of the following - lab documentation must be submitted: a. The member's platelet count is less than 30,000 x10^9/L b. The member has symptomatic bleeding or increased risk for bleeding and platelet count is less than 50,000 3. The member does not have a history of thrombosis or a genetic prothrombotic condition (e.g., Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency, or Protein C or S deficiency) 4. Avatrombopag is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz), or another thrombopoietin receptor agonist (e.g., eltrombopag [Alvaiz, Promacta], romiplostim [Nplate], lusutrombopag [Mulpleta]) 5. The dosage does not exceed the following: a. Adults and pediatrics 6 years and older: 40 mg tablet once daily and will be achieved using the fewest number of tablets per day b. Pediatric patients 1 year to less than 6 years: 20 mg oral granules once daily **Approval duration**: Chronic liver disease -- 60 days; Chronic ITP – 6 months
Eltrombopag choline (Alvaiz™)	**ALL** of the following are met (1 and 2); 1. The member has tried and had intolerable adverse effects to generic eltrombopag and **ALL** of the following must be submitted: a. The specific intolerance(s) and rationale for using Alvaiz must be specified b. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda c. Completed Naranjo Adverse Drug reaction probability scale - https://www.floridablue.com/docview/Naranjo-assessment-PDF/

	2. When used to treat thrombocytopenia associated with **ONE** of the following conditions and the member had an inadequate response to Promacta – documentation must be submitted: A. Persistent or Chronic immune (idiopathic) thrombocytopenic purpura (ITP) and **ALL** of the following are met: 1. The member has demonstrated an insufficient response to **EITHER** 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]) 2. The member does not have chronic liver disease 3. **ONE** of the following – lab documentation must be submitted: 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 4. Eltrombopag is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz), or another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 5. The dosage does not exceed 54 mg daily and will be achieved using the fewest number of tablets per day. B. Chronic hepatitis C virus (HCV) infection and **ALL** of the following are met: 1. The member's platelet count is less than 75,000 – lab documentation must be submitted 2. The intent of eltrombopag therapy is one of the following: a. To allow the member to initiate interferon-based therapy b. To allow the member to maintain interferon based therapy 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dosage does not exceed 72 mg daily and will be achieved using the fewest number of tablets per day. C. Severe aplastic anemia (SAA) and **ALL** of the following are met: 1. **ONE** of the following– lab documentation must be submitted:

	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 2. The member has demonstrated an insufficient response to immunosuppressive therapy (e.g.,anti-thymocyte globulin, cyclosporine) 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dosage does not exceed 108 mg daily and will be achieved using the fewest number of tablets per day. D. Low Risk Myelodysplastic Syndrome (MDS) (i.e., IPSS low and intermediate-1 categories; IPSS-R: Very low, low, intermediate categories; WPSS Very low, low, and intermediate categories) and ALL of the following: 1. **ONE** of the following– lab documentation must be submitted: i. The member's platelet count is less than 30,000 ii. The member has symptomatic bleeding or increased risk for bleeding and platelet count is less than 50,000 2. Eltrombopag is used as a single agent or in combination with one of the following: i. Anti-thymocyte globulin ii. Cyclosporine iii. Anti-thymocyte globulin and cyclosporine 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim, avatrombopag, lusutrombopag) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets or packets per day E. Thrombocytopenia post-hematopoietic cell transplant 1. The member's platelet count is less than 100,000 for 3 or more weeks following hematopoietic cell transplant – lab documentation must be submitted 2. Other potential causes of thrombocytopenia have been ruled out

	3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim, avatrombopag, lusutrombopag) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets per day F. Immune checkpoint inhibitor thrombocytopenia (ICI-T) 1. The member developed thrombocytopenia following the use of an immune-checkpoint inhibitor 2. The member had an inadequate response or contraindication to corticosteroids 3. ONE of the following – lab documentation must be submitted: i. The member's platelet count is less than 50,000 ii. The member's platelet count decreased greater than 50% from baseline 4. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim, avatrombopag, lusutrombopag) 5. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets per day. **Approval duration**: 6 months
Eltrombopag Olamine (Promacta®)	**ALL** of the following are met (1 and 2): 1.If the request is for brand Promacta, the member the member meets all of the following: i. The member has tried and had intolerable adverse effects to generic eltrombopag and **ALL** of the following must be submitted: a. The specific intolerance(s) and rationale for using brand Promacta must be specified b. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda c. Completed Naranjo Adverse Drug reaction probability scale -

	https://www.floridablue.com/docview/Naranjo-assessment-PDF/ 2. Eltrombopag is used to treat thrombocytopenia associated with **ONE** of the following conditions: A. Persistent or Chronic immune (idiopathic) thrombocytopenic purpura (ITP) and **ALL** of the following are met: 1. The member has demonstrated an insufficient response to **ONE** 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]) 2. **ONE** of the following – lab documentation must be submitted: 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. Eltrombopag is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz), or another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dosage does not exceed 75 mg daily and will be achieved using the fewest number of tablets or packets per day. B. Chronic hepatitis C virus (HCV) infection and **ALL** of the following are met: 1. The member's platelet count is less than 75,000 – lab documentation must be submitted 2. The intent of eltrombopag therapy is one of the following: a. To allow the member to initiate interferon-based therapy b. To allow the member to maintain interferon based therapy 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dosage does not exceed 100 mg daily and will be achieved using the fewest number of tablets or packets per day. C. Severe aplastic anemia (SAA) and ALL of the following are met:

	1. **ONE** of the following- lab documentation must be submitted: 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 2. **ONE** of the following: a. The member has demonstrated an insufficient response to immunosuppressive therapy (e.g.,anti-thymocyte globulin, cyclosporine) b. The member will receive treatment in combination with immunosuppressive therapy (i.e.,antithymocyte globulin, cyclosporine) 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dosage does not exceed 150 mg daily and will be achieved using the fewest number of tablets or packets per day. D. Low Risk Myelodysplastic Syndrome (MDS) (i.e., IPSS low and intermediate-1 categories; IPSS-R: Very low, low, intermediate categories; WPSS Very low, low, and intermediate categories) and **ALL** of the following: 1. **ONE** of the following- lab documentation must be submitted: i. The member's platelet count is less than 30,000 ii. The member has symptomatic bleeding or increased risk for bleeding and platelet count is less than 50,000 2. Eltrombopag is used as a single agent or in combination with one of the following: i. Anti-thymocyte globulin ii. Cyclosporine iii. Anti-thymocyte globulin and cyclosporine 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim, avatrombopag, lusutrombopag) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets or packets per day. E. Thrombocytopenia post-hematopoietic cell transplant

	1. The member's platelet count is less than 100,000 for 3 or more weeks following hematopoietic cell transplant – lab documentation must be submitted 2. Other potential causes of thrombocytopenia have been ruled out 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim, avatrombopag, lusutrombopag) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets or packets per day. F. Immune checkpoint inhibitor thrombocytopenia (ICI-T) 1. The member developed thrombocytopenia following the use of an immune-checkpoint inhibitor 2. The member had an inadequate response or contraindication to corticosteroids 3. ONE of the following – lab documentation must be submitted: i. The member's platelet count is less than 50,000 ii. The member's platelet count decreased greater than 50% from baseline 4. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim, avatrombopag, lusutrombopag) 5. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets or packets per day. **Approval duration**: 6 months
Fostamatinib (Tavalisse®)	**ALL** of the following: 1.Chronic immune (idiopathic) thrombocytopenic purpura (ITP) and **ALL** of the following are met: A.The member has demonstrated an insufficient response to **ONE or more** of the following: c. Adequate trial of corticosteroids (e.g., prednisone 1-2 mg/kg for 2-4 weeks)

	d. Immunoglobulins therapy (e.g., intravenous immune globulin [IVIG]) e. Thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Promacta], avatrombopag [Doptelet]) B.**ONE** of the following – lab documentation must be submitted: 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 5. Fostamatinib is not used concurrently with chronic immune globulin therapy, rituximab, rilzabrutinib (Wayrilz), or a thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Alvaiz, Promacta], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 6. The dosage does not exceed 300 mg daily and will be achieved using the fewest number of tablets per day. **Approval duration**: 6 months
Lusutrombopag (Mulpleta®)	**ALL** of with the following: A.Chronic liver disease (CLD) and **ALL** of the following are met: 1.The member's platelet count is less than 50 x10^9L – lab documentation must be submitted 2.The member is scheduled to undergo an elective procedure with an associated risk of bleeding that would require a platelet transfusion 3.The elective procedure is scheduled to occur 8 to 14 days after initiation of therapy with lusutrombopag 4.The member dose not have a history of thrombosis or a genetic prothrombotic condition (e.g., Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency, or Protein C or S deficiency) 5.The member had an inadequate response or intolerance to avatrombopag (Doptelet)† 6.Lusutrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., avatrombopag [Doptelet®], romiplostim [Nplate™], eltrombopag [Promacta]) 7. The dosage does not exceed 3 mg once daily for 7 days **Approval duration**: 60 days

	†Step therapy requirement does not apply if a prior health plan paid for the medication - documentation of a paid claim within the past 90 days must be submitted
Rilzabrutinib (Wayrilz)	**ALL** of the following: 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 – documentation must be submitted: 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]) 2.The member has demonstrated an insufficient response to a thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Promacta], avatrombopag [Doptelet]) – documentation must be submitted 3.**ONE** of the following – lab documentation must be submitted: 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 4.Rilzabrutinib is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse®), or a thrombopoietin receptor agonist (e.g., eltrombopag [Alvaiz, Promacta], romiplostim [Nplate], lusutrombopag [Mulpleta]) 5.The dosage does not exceed 400 mg twice daily and will be achieved using the fewest number of tablets per day. **Approval duration**: 6 months

II. Continuation of the requested agent **meets the definition of medical necessity** when used for the treatment of **ONE** of the following conditions in Table 2 and **ALL** of the associated criteria are met:

Avatrombopag (Doptelet, Doptelet Sprinkle),	**ALL** of the following are met: A. The member has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of chronic ITP, **OR** the member has previously met all indication-specific criteria B. The member has a beneficial response to therapy evidenced by an improvement in platelet count from baseline – lab documentation must be submitted C. Avatrombopag is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz), or another thrombopoietin receptor agonist (e.g., eltrombopag [Alvaiz, Promacta], romiplostim [Nplate], or lusutrombopag [Mulpleta]) D. The dose does not exceed the following: a. Adults and pediatric patients 6 years and older: 40 mg tablet once daily and will be achieved using the fewest number of tablets per day. b. Pediatric patients 1 year to less than 6 years: 20 mg oral granules once daily **Approval duration**: Chronic ITP – 1 year

Eltrombopag choline (Alvaiz™)	**ALL** of the following are met (1 and 2): 1. The member has tried and had intolerable adverse effects to generic eltrombopag and **ALL** of the following must be submitted: a. The specific intolerance(s) and rationale for using Alvaiz must be specified b. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda c. Completed Naranjo Adverse Drug reaction probability scale - https://www.floridablue.com/docview/Naranjo-assessment-PDF/ 2. When used for treatment of thrombocytopenia associated with one of the following conditions and **ALL** of the condition-specific criteria are met: A. Persistent or Chronic ITP 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of persistent or 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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz), or another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed 54 mg daily and will be achieved using the fewest number of tablets per day. B.Chronic HCV infection 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of chronic HCV infection, **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 – lab documentation must be submitted

	3. The member is receiving concomitant interferon-based therapy 4. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 5. The dose does not exceed 72 mg daily and will be achieved using the fewest number of tablets per day. C.Severe aplastic anemia 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of severe aplastic anemia, **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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed 108 mg daily and will be achieved using the fewest number of tablets per day. D.Low Risk Myelodysplastic Syndrome (MDS) and **ALL** of the following: 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of MDS, **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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets per day. E.Thrombocytopenia post-hematopoietic cell transplant and **ALL** of the following: 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for

	eltrombopag for the treatment of thrombocytopenia post-hematopoietic cell transplant, **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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets per day. F.Immune checkpoint inhibitor thrombocytopenia (ICI-T) and **ALL** of the following: 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of ICI-T, 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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets per day. **Approval duration**: 1 year

Eltrombopag Olamine (Promacta®)	**ALL** of the following are met (1 and 2): 1.If the request is for brand Promacta, the member the member meets all of the following: i. The member has tried and had intolerable adverse effects to generic eltrombopag and **ALL** of the following must be submitted: a. The specific intolerance(s) and rationale for using brand Promacta must be specified b. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda c. Completed Naranjo Adverse Drug reaction probability scale - https://www.floridablue.com/docview/Naranjo-assessment-PDF/ 2.When used for the treatment of thrombocytopenia associated with one of the following conditions and **ALL** of the condition-specific criteria are met: A. Persistent or Chronic ITP 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of persistent or 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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz), or another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed 75 mg daily and will be achieved using the fewest number of tablets or packets per day. B. Chronic HCV infection 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of chronic HCV

	infection, **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 – lab documentation must be submitted 3. The member is receiving concomitant interferon-based therapy 4. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 5. The dose does not exceed 100 mg daily and will be achieved using the fewest number of tablets or packets per day. C. Severe aplastic anemia 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of severe aplastic anemia, **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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed 150 mg daily and will be achieved using the fewest number of tablets or packets per day. D. Low Risk Myelodysplastic Syndrome (MDS) and **ALL** of the following: 1.The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of MDS, **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 – lab documentation must be submitted 3.Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim

	[Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4.The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets or packets per day. E. Thrombocytopenia post-hematopoietic cell transplant and **ALL** of the following: 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of thrombocytopenia post-hematopoietic cell transplant, 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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets or packets per day. F. Immune checkpoint inhibitor thrombocytopenia (ICI-T) and **ALL** of the following: 1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for eltrombopag for the treatment of ICI-T, 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 – lab documentation must be submitted 3. Eltrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 4. The dose does not exceed the maximum FDA-approved dose and will be achieved using the fewest number of tablets or packets per day. **Approval duration**: 1 year

Fostamatinib (Tavalisse®)	**ALL** of the condition-specific criteria are met: 1.Chronic ITP A.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 B.The member has a beneficial response to therapy evidenced by an improvement in platelet count from baseline – lab documentation must be submitted C.Fostamatinib is not used concurrently with chronic immune globulin therapy, rituximab, rilzabrutinib (Wayrilz), or a thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Alvaiz, Promacta], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) D.The dose does not exceed 300 mg daily and will be achieved using the fewest number of tablets per day. **Approval duration**: 1 year

Rilzabrutinib (Wayrilz)	**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 rilzabrutinib for the treatment of chronic ITP (if another health plan, documentation of a health plan-paid claim during the 90 days immediately before the authorization request must be provided), **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 – lab documentation must be submitted 3.Rilzabrutinib is not used concurrently with chronic immune globulin therapy, rituximab, or fostamatinib (Tavalisse), or a thrombopoietin receptor agonist (e.g., eltrombopag [Alvaiz, Promacta], romiplostim [Nplate], lusutrombopag [Mulpleta]) 4.The dose does not exceed 400 mg twice 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:

Eltrombopag is indicated for the treatment of thrombocytopenia in adult and pediatric patients 1 year and older with persistent or chronic immune thrombocytopenia (ITP) with an insufficient response to corticosteroids, immunoglobulins, or splenectomy. It is also indicated for thrombocytopenia in patients with chronic hepatitis C virus (HCV) to allow the initiation and maintenance of interferon-based therapy. Eltrombopag is indicated for patients with severe aplastic anemia in adult and pediatric patients 2 years and older as first line therapy (Promacta only) in combination with immunosuppressants (antithymocyte globulin and cyclosporine) and as subsequent therapy (Promacta and Alvaiz) in those who have had an insufficient response to immunosuppressive therapy.

Dose adjustments are based upon the platelet count response. Do not use eltrombopag in an attempt to normalize platelet counts.

Eltrombopag should be administered without a meal or with a meal low in calcium (≤50 mg). Take at least 2 hours before or 4 hours after other medications (e.g., antacids), calcium-rich foods (e.g., dairy products and calcium fortified juices), or supplements containing polyvalent cations such as iron, calcium, aluminum, magnesium, selenium, and zinc. Do not split, chew or crush tablets. See prescribing information for preparation of the oral suspension.

ITP

Promacta

- Initial dose: 50 mg once daily for most adult patients and pediatric patents 6 years of age and older and 25 mg once daily for pediatric patients aged 1 to 5 years. Dose reductions are needed in persons of East Asian ancestry (such as Chinese, Japanese, Taiwanese, or Korean) or who have mild to severe hepatic impairment (Child-Pugh Class A, B, C).

  - East Asian ancestry, initiate eltrombopag at a reduced dose of 25 mg once daily.

  - Mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, C), initiate eltrombopag at a reduced dose of 25 mg once daily.

  - East Asian ancestry with hepatic impairment (Child-Pugh Class A, B, C), initiate eltrombopag at a reduced dose of 12.5 mg once daily.

- Use the lowest dose of eltrombopag to achieve and maintain a platelet count ≥50,000 as necessary to reduce the risk for bleeding.
- Do not exceed a dose of 75 mg daily.
- See prescribing information for dose adjustment and monitoring.

HCV

Promacta

Use the lowest dose of eltrombopag to achieve and maintain a platelet count necessary to initiate and maintain antiviral therapy with pegylated interferon and ribavirin. Dose adjustments are based upon the platelet count response. Do not use eltrombopag to normalize platelet counts.

- Initial Dose: Initiate eltrombopag at a dose of 25 mg once daily.
- Monitoring and Dose Adjustment: Adjust the dose of eltrombopag in 25 mg increments every 2 weeks as necessary to achieve the target platelet count required to initiate antiviral therapy. Monitor platelet counts every week prior to starting antiviral therapy.
- During antiviral therapy, adjust the dose of eltrombopag to avoid dose reductions of peginterferon. Monitor CBCs with differentials (including platelet counts) weekly during antiviral therapy until a stable platelet count is achieved. Monitor platelet counts monthly thereafter. Do not exceed a dose of 100 mg daily. Monitor clinical hematology and liver tests regularly throughout therapy with eltrombopag.
- See prescribing information for dose adjustment and monitoring.

SAA

Promacta

First line therapy:

Initiate concurrently with standard immunosuppressive therapy (antithymocyte globulin and cyclosporine). For patients 12 years and older initiate at 150 mg once daily for 6 months. For pediatric patients 6 to 11 years initiate at 75 mg once daily for 6 months. For pediatric patients aged 2 to 5 years 2.5 mg/kg once daily for 6 months.

See prescribing information for initial dose adjustment for patients of Asian ancestry, or those with mild moderate, or severe hepatic impairment. Adjust initial dose if baseline ALT or AST levels are abnormal.

The dose should be modified based on platelet counts, ALT, or AST elevations. The duration of treatment is 6 months.

Refractory SAA:

Promacta

Use the lowest dose of eltrombopag to achieve and maintain a platelet count necessary to maintain a hematologic response. Dose adjustments are based upon the platelet count response. Hematologic response requires dose titration.

- Initial dose: 50 mg once daily, except in persons of East Asian ancestry (such as Chinese, Japanese, Taiwanese, or Korean) or who have mild to severe hepatic impairment (Child-Pugh Class A, B, C).

    - East Asian ancestry, initiate eltrombopag at a reduced dose of 25 mg once daily.

    - Mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, C), initiate eltrombopag at a reduced dose of 25 mg once daily.

- After initiating eltrombopag,adjust the dose every 2 weeks as necessary to achieve and maintain a platelet count ≥50,000.
- Do not exceed a dose of 150 mg daily.
- See prescribing information for dose adjustment and monitoring.

ITP

Alvaiz

- Initial dose: 36 mg once daily for most adult patients and pediatric patents 6 years of age and older. Dose reductions are needed in persons of East Asian ancestry (such as Chinese, Japanese, Taiwanese, or Korean) or who have mild to severe hepatic impairment (Child-Pugh Class A, B, C).

    - East Asian ancestry, initiate eltrombopag at a reduced dose of 18 mg once daily.

    - Mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, C), initiate eltrombopag at a reduced dose of 18 mg once daily.

- East Asian ancestry with hepatic impairment (Child-Pugh Class A, B, C), initiate eltrombopag at a reduced dose of 9 mg once daily.

- Use the lowest dose of eltrombopag to achieve and maintain a platelet count ≥50,000 as necessary to reduce the risk for bleeding.
- Do not exceed a dose of 54 mg daily.
- See prescribing information for dose adjustment and monitoring.

HCV

Alvaiz

Use the lowest dose of eltrombopag to achieve and maintain a platelet count necessary to initiate and maintain antiviral therapy with pegylated interferon and ribavirin. Dose adjustments are based upon the platelet count response. Do not use eltrombopag to normalize platelet counts.

- Initial Dose: Initiate eltrombopag at a dose of 18 mg once daily.
- Monitoring and Dose Adjustment: Adjust the dose of eltrombopag in 18 mg increments every 2 weeks as necessary to achieve the target platelet count required to initiate antiviral therapy. Monitor platelet counts every week prior to starting antiviral therapy.
- During antiviral therapy, adjust the dose of eltrombopag to avoid dose reductions of peginterferon. Monitor CBCs with differentials (including platelet counts) weekly during antiviral therapy until a stable platelet count is achieved. Monitor platelet counts monthly thereafter. Do not exceed a dose of 72 mg daily. Monitor clinical hematology and liver tests regularly throughout therapy with eltrombopag.
- See prescribing information for dose adjustment and monitoring.

Refractory SAA:

Alvaiz

Use the lowest dose of eltrombopag to achieve and maintain a platelet count necessary to maintain a hematologic response. Dose adjustments are based upon the platelet count response. Hematologic response requires dose titration.

- Initial dose: 36 mg once daily, except in persons of East Asian ancestry (such as Chinese, Japanese, Taiwanese, or Korean) or who have mild to severe hepatic impairment (Child-Pugh Class A, B, C).

    - East Asian ancestry, initiate eltrombopag at a reduced dose of 18 mg once daily.

    - Mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, C), initiate eltrombopag at a reduced dose of 18 mg once daily.

- After initiating eltrombopag,adjust the dose every 2 weeks as necessary to achieve and maintain a platelet count ≥50,000.
- Do not exceed a dose of 108 mg daily.

- See prescribing information for dose adjustment and monitoring.

Doptelet

Thrombocytopenia in Chronic Liver Disease scheduled to undergo a procedure: Thrombocytopenia in adult patients with chronic liver disease scheduled to undergo a procedure should begin dosing 10 to 13 days prior to a scheduled procedure. Patients should undergo the procedure within 5 to 8 days after the last dose. Take with food once daily for 5 consecutive days and dose is based on platelet count prior to a scheduled procedure. Obtain platelet count prior to administration and on the day of the scheduled procedure to ensure adequate platelet response.

- Platelet count less than 40 $x10^9$/L: 60 mg (3 tablets) daily for 5 days
- Platelet count greater than or equal to 40 $x10^9$/L to less than 50 $x10^9$/L: 40 mg (2 tablets) daily for 5 days

Thrombocytopenia in chronic immune thrombocytopenia (ITP): Thrombocytopenia in adult and pediatric patients 6 years and older with chronic ITP who have had an insufficient response to a previous treatment should begin 20 mg once daily and adjust the dose or frequency of dosing to maintain platelet count greater than or equal to 50 x 10^9/L. Assess platelets weekly until a stable platelet count is achieved and then monthly thereafter. Obtain platelet counts at least 4 weeks following discontinuation. Dose adjust based on the platelet response (see prescribing information for dose level 1 through 6). Do not exceed 40 mg per day. Discontinue if platelet count does not increase to greater than 50 x 10^9/L after 4 weeks of dosing at the maximum dose. Discontinue if the platelet count is greater than 400 x 10^9/L after 2 weeks of dosing at 20 mg once weekly.

Thrombocytopenia in pediatric patients 1 year to less than 6 years with persistent or chronic immune thrombocytopenia who have had an insufficient response to a previous treatment: Initiate oral granules at 10 mg orally once daily. Adjust the dose or frequency of dosing to maintain platelet count greater than or equal to 50 x 10^9/L. Do not exceed 20 mg (2 capsules) per day. See prescribing information.

Mulpleta

Thrombocytopenia in adult patients with chronic liver disease scheduled to undergo a procedure should begin dosing 8 to 14 days prior to a scheduled procedure. Patients should undergo the procedure within 2 to 8 days after the last dose. Take 3 mg with or without food once daily for 7 consecutive days prior to a scheduled procedure. Obtain platelet count prior to administration and not more than 2 days before the scheduled procedure to ensure adequate platelet response.

Tavalisse

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. See prescribing information for dose adjustments for adverse reactions and drug interations.

Wayrilz

For treatment of thrombocytopenia in adults with persistent or chronic immune thrombocytopenia purpura (ITP) who have had an insufficient response to a previous treatment: 400 mg twice daily.

Drug Availability:

- **Alvaiz**: 9 mg, 18 mg, 36 mg, and 54 mg tablets
- **Doptelet:** 20 mg tablets
- **Doptelet Sprinkle:** 10 mg oral granules
- **Mulpleta:** 3 mg tablets
- **Promacta (eltrombopag olamine)**: 12.5 mg, 25 mg, 50 mg, 75 mg tablets, and is also available as a 12.5 mg and 25 mg packet for oral suspension.
- **Tavalisse:** 100 mg and 150 mg tablets
- **Wayrilz:** 400 mg tablets

PRECAUTIONS:

Boxed Warning:

Eltrombopag may cause hepatic decompensation in patients with chronic hepatitis C and risk of hepatotoxicity. When used in combination with interferon and ribavirin in persons with chronic HCV infection, eltrombopag may increase the risk of hepatic decompensation. The risk of severe and potentially life-threatening hepatotoxicity is increased with eltrombopag. Monitor hepatic function and discontinue dosing as recommended.

- Measure serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin prior to initiation of eltrombopag, every 2 weeks during the dose adjustment phase, and monthly following establishment of a stable dose. If bilirubin is elevated, perform fractionation.
- Evaluate abnormal serum liver tests with repeat testing within 3 to 5 days. If the abnormalities are confirmed, monitor serum liver tests weekly until the abnormality(ies) resolve, stabilize, or return to baseline levels.
- Discontinue eltrombopag if ALT levels increase to ≥3X upper limit of normal (ULN) in persons with normal liver function or ≥3X (or greater than 5 x ULN, whichever is lower) baseline in persons with pre-treatment elevations in transaminases and are:
    - progressively increasing, or
    - persistent for ≥4 weeks, or
    - accompanied by increased direct bilirubin, or
    - accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation

Warnings/Precautions:

Eltrombopag

Hepatotoxicity: monitor liver function before and during therapy.

Hepatic decompensation: hepatic decompensation can occur in persons with chronic hepatitis C infection.

Monitor persons with low albumin levels or with a MELD score of 10 or greater at baseline.

Increased risk of death and progression of Myelodysplastic Syndromes (MDS) to Acute Myeloid Leukemia (AML): A trial in patients with IPSS intermediate-1, intermediate-2 or high risk MDS with thrombocytopenia with azacitidine in combination with either eltrombopag or placebo was terminated due to lack of efficacy and safety.

Thrombotic/thromboembolic complications: portal vein thrombosis has been reported in persons with chronic liver disease receiving eltrombopag. Monitor platelet counts regularly.

Cataracts: monitor patients regularly for signs and symptoms of cataracts developing or worsening.

Lab test interference: highly colored and can cause patient sample discoloration which can interfere with some lab tests (e.g., bilirubin and creatinine).

Doptelet

- Thrombotic and thromboembolic complications in patients with chronic liver disease or chronic ITP have been associated with thrombopoietin receptor agonists. Consider thrombotic risk when administering to patients with known risk factors for thromboembolism including genetic prothrombotic conditions (Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency, or Protein C or S deficiency). Monitor platelet counts and for thromboembolic events.
- Do not administer to patients with chronic liver disease to normalize platelet counts.

Multpleta

- Thrombotic and thromboembolic complications in patients with chronic liver disease have been associated with thrombopoietin receptor agonists. Consider thrombotic risk when administering to patients with known risk factors for thromboembolism including genetic prothrombotic conditions (Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency, or Protein C or S deficiency). Monitor platelet counts and for thromboembolic events. In patients with ongoing or prior thrombosis or absence of hepatopetal blood flow, only use if the potential benefit justifies the potential risk. Do not administer to patients with chronic liver disease to normalize platelet counts.

Tavalisse

- 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.

Wayrilz

- Serious Infections: Monitor patients for signs and symptoms of infection, evaluate promptly, and treat.
- Hepatotoxicity, Including Drug-Induced Liver Injury: Evaluate bilirubin and transaminases at baseline and as clinically indicated during treatment.
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk and to use effective contraception.

BILLING/CODING INFORMATION:

HCPCS Coding

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

ICD-10 Diagnosis Codes That Support Medical Necessity

B18.0 – B18.9	Chronic viral hepatitis
C22.0	Hepatocellular carcinoma
C93.10	Chronic myelomonocytic leukemia
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20 – D46.21	Refractory anemia with excess of blasts
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.Z	Other myelodysplastic syndromes
D61.09	Other constitutional aplastic anemia
D61.1	Drug-induced aplastic anemia
D61.2	Aplastic anemia due to other external agents
D61.3	Idiopathic aplastic anemia
D61.89	Other specified aplastic anemias and other bone marrow failure syndromes
D61.9	Aplastic anemia, unspecified
D69.3	Immune thrombocytopenic purpura
K70.0 – K70.9	Alcoholic liver disease
K73.0 – K73.9	Chronic hepatitis, not elsewhere classified
K74.0 – K74.69	Fibrosis and cirrhosis of liver
K75.81	Nonalcoholic steatohepatitis
K76.9	Chronic nonalcoholic liver disease

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 last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

International Prognostic Scoring System (IPSS): classification system used in staging individuals with MDS. The IPSS evaluates three components when determining an overall score of 0 to 2.5: percent marrow blasts, cytogenics (e.g., del(5)q chromosome), and cytopenias. An IPSS score of 0 corresponds to low risk, 0.5-1 to intermediate risk 1, 1.5-2 to intermediate risk 2, and 2.5 or greater to high risk.

IPSS Classification System	
Risk Level	IPSS Score
Low risk	0
Intermediate risk 1	0.5-1
Intermediate risk 2	1.5-2
High risk	2.5 or greater

The following factors are used to calculate the IPSS score

	0	0.5	1.0	1.5	2.0
% Marrow Blasts	Less than 5	5-10		11-20	21-30
Cytogenetics	Normal, -Y, del(5)g alone, del(20)q alone	Other	-7, del (7)q, 3 or more abnormalities		
Cytopenias • Hemoglobin <10 g/dL Neutrophil count less than 1800/mcL	Only 1	Two of the three			

• Platelet count less than 100,000 cells/mm3					
ANC, absolute neutrophil count					

Myelodysplastic Syndrome (MDS): any of a group of related bone marrow disorders of varying duration preceding the development of overt acute myelogenous leukemia; they are characterized by abnormal hematopoietic stem cells, anemia, neutropenia and thrombocytopenia. Also called releukemia.

Revised International Prognostic Scoring System (IPSS-R): classification system used in staging individuals with MDS. Individuals are assigned to 1 of 5 risk groups.

IPSS-R Classification System	
Risk Level	IPSS-R Score
Very Low	≤1.5
Low	>1.5- ≤3
Intermediate	>3 - ≤4.5
High	>4.5 - ≤6
Very High	>6

The following factors are used to calculate the IPSS-R score

Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetics	Very good	-	Good	-	Intermediate	Poor	Very poor
% Marrow Blasts	≤2	-	>2 - <5	-	5-10	>10	-
Hemoglobin	≥10	-	8 - <10	< 8			
Platelets	≥100	50 - <100	<50	-	-	-	-
ANC	≥0.8	<0.8	-	-	-	-	-
ANC, absolute neutrophil count							

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.

World Health Organization (WHO) Prognostic Scoring System (WPSS): classification system used in staging individuals with MDS. This system is based on the WHO classification of the MDS subtype, karyotype, and presence of severe anemia. Individuals are assigned to 1 of 5 risk groups and the risk category may change over the course of the disease.

WPSS Classification System				
	Score			
Variable	0	1	2	3

WHO Category	RCUD, RARS, MDS with isolated del (5q)	RCMD	RAEB-1	RAEB-2
Karyotype	Good	Intermediate	Poor	--
Severe anemia (hemoglobin <9 g/dL in males or <8 g/dL in females)	Absent	Present	--	--
RCUD, refractory cytopenia with unilineage dysplasia (includes refractory anemia, refractory neutropenia, and refractory thrombocytopenia); RAEB, refractory anemia with excess blasts; RARS, refractory anemia with ringed sideroblasts; RCMD, refractory cytopenia with multilineage dysplasia; A score of 0=very low risk, 1= low risk, 2=intermediate risk, 3-4=high risk, 5-6=very high risk				

RELATED GUIDELINES:

Immune Globulin Therapy, 09-J0000-06
Rituximab (Rituxan®), 09-J0000-59
Romiplostim Injection (Nplate™), 09-J0000-88

OTHER:

None.

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9. Tavalisse (fostamatinib) [package insert]. Rigel Pharmaceuticals, Inc. South San Francisco, CA: Nov 2020.
10. Wayrilz (rilzabrutinib) [package insert]. Genzyme Corporation. Cambridge, MA: Aug 2025

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 2/11/26.

GUIDELINE UPDATE INFORMATION:

3/15/26	Consolidation of thrombocytopenia oral therapy into a single medical coverage guideline.