



PHARMACY COVERAGE GUIDELINES  
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 8/02/18  
LAST REVIEW DATE: 8/15/19  
LAST CRITERIA REVISION DATE: 8/15/19  
ARCHIVE DATE:

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**DOPTELET® (avatrombopag) oral tablet**  
**MULPLETA® (lusutrombopag) oral tablet**  
**PROMACTA® (eltrombopag) oral tablet and oral suspension**  
**TAVALISSE™ (fostamatinib) oral tablet**

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Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

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Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com). **Incomplete forms or forms without the chart notes will be returned.**

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## **Section A. Chronic Liver Disease associated thrombocytopenia, pre-procedural use:**

### **Doptelet (avatrombopag)** **Mulpleta (lusutrombopag)**

- **Criteria for therapy:** Doptelet (avatrombopag) and Mulpleta (lusutrombopag) are considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
1. Prescriber is a physician specializing in platelet disorders or is in consultation with Gastroenterologist, Hepatologist, Hematologist, or Transplantation Specialist (when appropriate)
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of **thrombocytopenia** in an individual with **chronic liver disease scheduled to undergo an elective procedure** and the degree of thrombocytopenia and clinical condition increases the risk for bleeding **OR** has documented bleeding symptoms
  4. Individual has failure, contraindication or intolerance to **BOTH** the following preferred step therapy agents:
    - Dexamethasone
    - Methylprednisolone
  5. Platelet count at 8-14 days before the scheduled procedure is less than  $50 \times 10^9/L$
  6. Will not be used in an attempt to normalize platelet count
  7. **ONE** of the following:
    - **Doptelet (avatrombopag)** will not be used in neurosurgical interventions, thoracotomy, laparotomy, or organ resection
    - **Mulpleta (lusutrombopag)** will not be used in patients undergoing thoracotomy, laparotomy, organ resection, open-heart surgery, or craniotomy, history of splenectomy, partial splenic

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embolization, or thrombosis, patients with Child Pugh Class-C, absence of hepatopetal blood flow, or a prothrombotic condition other than liver disease

8. Will not be used in combination with each other or with Promacta (eltrombopag), Tavalisse (fostamatinib), or Nplate (romiplostim) injection

**Approval duration:**

**For Doptelet:** 5-day supply per procedure, no refills

**For Mulpleta:** 7-day supply per procedure, no refills

**Section B. Chronic immune (idiopathic) thrombocytopenia (ITP):**

**Doptelet (avatrombopag)**  
**Promacta (eltrombopag)**  
**Tavalisse (fostamatinib)**

- **Criteria for initial therapy:** Doptelet (avatrombopag), Promacta (eltrombopag), or Tavalisse (fostamatinib) is considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
1. Prescriber is a physician specializing in platelet disorders or is in consultation with Hematologist or Transplantation Specialist (when appropriate)
  2. Individual age is **ONE** of the following:
    - **For Doptelet (avatrombopag):** 18 years of age or older
    - **For Promacta (eltrombopag):** 1 year of age or older
    - **For Tavalisse (fostamatinib):** 18 years of age or older
  3. A confirmed diagnosis of **chronic immune (idiopathic) thrombocytopenia (ITP)** and the degree of thrombocytopenia and clinical condition increases the risk for bleeding **OR** has documented bleeding symptoms
  4. Individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **TWO** the following preferred step therapy agents:
    - Corticosteroid [**EITHER** dexamethasone, methylprednisolone, or prednisone]
    - Immunoglobulin [**EITHER** IVIG or Anti-D (Rho)]
    - Splenectomy or is not a candidate for splenectomy
    - Azathioprine
    - Danazol

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5. **Additional criteria for Doptelet (avatrombopag) and Tavalisse (fostamatinib) only:**
  - Has failure, contraindication or intolerance to Promacta (eltrombopag)
6. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
  - **For Doptelet (avatrombopag):**
    - Platelet count is less than  $50 \times 10^9/L$  or has documented bleeding symptoms
  - **For Promacta (eltrombopag):**
    - Platelet count is less than  $50 \times 10^9/L$  or has documented bleeding symptoms
    - Complete blood count
    - Liver function tests
    - Ocular examination for detection of cataracts
  - **For Tavalisse (fostamatinib):**
    - Platelet count is less than  $50 \times 10^9/L$  or has documented bleeding symptoms
    - Complete blood count
    - Liver function tests
    - Blood pressure, if abnormal, antihypertensive medication(s) have been initiated or adjusted
    - Negative pregnancy test in a woman of child bearing potential
7. Will not be used to normalize platelet count and will not be used if the platelet count is greater than  $400 \times 10^9/L$
8. Will not be used in combination with each other or with Mulpleta (lusutrombopag) or Nplate (romiplostim) injection

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Doptelet (avatrombopag), Promacta (eltrombopag), or Tavalisse (fostamatinib) is considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
1. Individual continues to be seen by a physician specializing in platelet disorders or is in consultation with a Hematologist or Transplantation Specialist (when appropriate)
  2. Individual's condition responded while on therapy
    - Response is defined as **ALL** of the following:
      - Achieved and maintains a platelet count of  $\geq 50 \times 10^9/L$

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- Has not had any platelet transfusions, fresh frozen plasma, whole blood, packed red blood cells, cryoprecipitate, vitamin K, desmopressin, recombinant activated factor VII, aminocaproic acid, tranexamic acid, surgical or interventional radiology procedure to control blood loss
  - Has not had any serious or severe bleeding events
  - Has not had any hospitalizations for severe thrombocytopenia
3. Individual has been adherent with the medication
  4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
    - Significant adverse effect such as:
      - For: Doptelet (avatrombopag):
        - Thrombotic or thromboembolic complications (arterial or venous)
      - For Promacta (eltrombopag):
        - Thrombotic/thromboembolic complications (arterial or venous)
        - Persistent platelet count > 400 x 10<sup>9</sup>/L
        - Hyperbilirubinemia
        - Hepatotoxicity, liver injury or persistent elevation of LFT's or hepatic decompensation
        - Development or worsening of cataracts
      - For Tavalisse (fostamatinib):
        - Severe hypertension despite 4 weeks of aggressive antihypertensive therapy
        - Hypertensive crisis (SBP > 180 and/or DBP > 120 mmHg) despite 4 weeks of aggressive therapy
        - Hepatotoxicity (AST/ALT persist at 5 x ULN or higher for 2 weeks or more **OR** AST/ALT is 3 x ULN or more **AND** total bilirubin is greater than 2 x ULN)
        - Persistent severe diarrhea despite use of antidiarrheal agents
        - Persistent neutropenia (neutrophil count < 1 x 10<sup>9</sup>/L) despite dose adjustment
        - Unable to use at least 100 mg daily
  5. Will not be used to normalize platelet count and will not be used if the platelet count is greater than 400 x 10<sup>9</sup>/L
  6. Will not be used in combination with each other or with Mulpleta (lusutrombopag) or Nplate (romiplostim) injection
  7. There are no significant interacting drugs

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Renewal duration: 12 months

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### **Section C. Thrombocytopenia from Severe Aplastic Anemia:**

#### **Promacta (eltrombopag)**

- **Criteria for initial therapy:** Promacta (eltrombopag) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
1. Prescriber is a physician specializing in platelet disorders or is in consultation with Hematologist or Transplantation Specialist (when appropriate)
  2. Individual 18 years of age
  3. A confirmed diagnosis ***thrombocytopenia from severe aplastic anemia*** and the degree of thrombocytopenia and clinical condition increases the risk for bleeding **OR** has documented bleeding symptoms
  4. Individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **TWO** of the following:
    - Antithymocyte globulin with Cyclosporine with or without a Corticosteroid
    - Antithymocyte globulin [Thymoglobulin, Atgam] with or without a Corticosteroid
    - Antithymocyte globulin with Cyclophosphamide with or without a Corticosteroid
    - Cyclosporine with Cyclophosphamide
    - Cyclophosphamide
  5. Will not be used to normalize platelet count
  6. **ALL** of the following baseline tests have been completed before initiation of treatment:
    - Platelet count is less than  $50 \times 10^9/L$  or has documented bleeding symptoms
    - Complete blood count
    - Liver function tests
    - Ocular examination for detection of cataracts
  7. Will not be used in combination with Doptelet (avatrombopag), Mulpleta (lusutrombopag), Tavalisse (fostamatinib), or Nplate (romiplostim) injection

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Promacta (eltrombopag olamine) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
1. Individual continues to be seen by a physician specializing in platelet disorders or is in consultation with a Hematologist or Transplantation (when appropriate)
  2. Individual continues to be seen in consultation with a specialist in either Hematology, Hepatology, Gastroenterology, Infectious disease, or Transplantation (when appropriate)
  3. Individual's condition responded and has not worsened while on therapy
    - Response is defined as **TWO** of the following:
      - Achieved and maintains a stable platelet count **or** platelet count increased  $20 \times 10^9/L$  above baseline
      - Hemoglobin increased by  $> 1.5 \text{ g/dL}$  **or** a reduction in  $\geq 4$  units of RBC
      - ANC increase of 100% **or** an ANC increase  $> 0.5 \times 10^9/L$
      - Has not had any serious or severe bleeding events requiring rescue with any of the following:
        - Has not had any platelet transfusions, fresh frozen plasma, whole blood, packed red blood cells, cryoprecipitate, vitamin K, desmopressin, recombinant activated factor VII, aminocaproic acid, tranexamic acid, surgical or interventional radiology procedure to control blood loss
      - Has not had any hospitalizations for severe thrombocytopenia
  4. Individual has been adherent with the medication
  5. Will not be used to normalize platelet count and will not be used if the platelet count is greater than  $400 \times 10^9/L$
  6. Will not be used in combination with Doptelet (avatrombopag), Mulpleta (lusutrombopag), Tavalisse (fotamatinib), or Nplate (romiplostim) injection
  7. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
    - Significant adverse effect such as:
      - Thrombotic/thromboembolic complications (arterial or venous)
      - Persistent platelet count  $>400 \times 10^9/L$
      - Hyperbilirubinemia
      - Hepatotoxicity, liver injury or persistent elevation of LFT's or hepatic decompensation
      - Development or worsening of cataracts
  8. There are no significant interacting drugs

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Renewal duration: 12 months

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## **Section D. Chronic hepatitis C thrombocytopenia from interferon-based therapy:**

### **Promacta (eltrombopag)**

- **Criteria for initial therapy:** Promacta (eltrombopag) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
1. Prescriber is a physician specializing in hepatitis C or is in consultation with a Hepatologist, Gastroenterologist, or Infectious disease
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of ***chronic hepatitis C in a candidate for interferon and ribavirin*** treatment but the degree of thrombocytopenia limits the ability to initiate interferon **OR** individual is on interferon-based therapy but the degree of thrombocytopenia limits the ability to continue interferon
  4. Individual is not at risk for hepatic decompensation
  5. Will not be used to normalize platelet count and will not be used if the platelet count is greater than  $400 \times 10^9/L$
  6. **ALL** of the following baseline tests have been completed before initiation of treatment:
    - Platelet count is less than  $50 \times 10^9/L$  or has documented bleeding symptoms
    - Complete blood count
    - Liver function tests
    - Ocular examination for detection of cataracts
  7. Will not be used in combination with Doptelet (avatrombopag), Mulpleta (lusutrombopag), Tavalisse (fotamatinib), or Nplate (romiplostim) injection

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Promacta (eltrombopag) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

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1. Individual continues to be seen by a physician specializing in hepatitis C or is in consultation with a Hepatologist, Gastroenterologist, or Infectious disease
2. Individual's condition responded while on therapy
  - Response is defined as:
    - Able to initiate interferon-based therapy **or** able to continue interferon-based therapy
    - Achieved and maintains a platelet count of  $50 \times 10^9/L$
    - Has not had any platelet transfusions, fresh frozen plasma, whole blood, packed red blood cells, cryoprecipitate, vitamin K, desmopressin, recombinant activated factor VII, aminocaproic acid, tranexamic acid, surgical or interventional radiology procedure to control blood loss
    - Has not had any serious or severe bleeding events
    - Has not had any hospitalizations for severe thrombocytopenia
3. Individual has been adherent with the medication
4. Continues with hepatitis C antiviral regimen of interferon and ribavirin, if this regimen is stopped, Promacta (eltrombopag) will not be renewed or continued
5. Will not be used to normalize platelet count and will not be used if the platelet count is greater than  $400 \times 10^9/L$
6. Will not be used in combination with Doptelet (avatrombopag), Mulpleta (lusutrombopag), Tavalisse (fostamatinib), or Nplate (romiplostim) injection
7. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
  - Significant adverse effect such as:
    - Thrombotic/thromboembolic complications (arterial or venous)
    - Persistent platelet count  $>400 \times 10^9/L$
    - Hyperbilirubinemia
    - Hepatotoxicity, liver injury or persistent elevation of LFT's or hepatic decompensation
    - Development or worsening of cataracts
8. There are no significant interacting drugs

**Renewal duration:** 6 months

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**Description:**

Doptelet (avatrombopag) and Mulpleta (lusutrombopag) are thrombopoietin (TPO) receptor agonist designed to mimic the effects of TPO. They are indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease (CLD) who are scheduled to undergo a procedure that would typically require platelet transfusion. Doptelet and Mulpleta should not be administered to patients with chronic liver disease in an attempt to normalize platelet counts. Doptelet is also indicated for chronic immune thrombocytopenia who have had an insufficient response to previous treatment.

When used as a pre-procedural agent, Doptelet dosing should begin 10-13 days prior to the scheduled procedure. The recommended daily dose of Doptelet is based on the patient's platelet count prior to the scheduled procedure. Patients should undergo their procedure 5-8 days after the last dose of Doptelet. Doptelet should be taken orally once daily for 5 consecutive days all five days of dosing should be completed. Doptelet has been investigated only as a single 5-day once daily dosing regimen in clinical trials in patients with chronic liver disease. The onset of the platelet count increase was observed in clinical trials was within 3-5 days of the start of a 5-day treatment course, with peak effect observed after 10-13 days. Subsequently, platelet counts decreased gradually, returning to near baseline values after 35 days. Patients undergoing neurosurgical interventions, thoracotomy, laparotomy, or organ resection were not studied in the Doptelet clinical trials.

Mulpleta dosing should begin 8-14 days prior to the scheduled procedure. The recommended daily dose of Mulpleta is 3 mg once daily. A platelet count should be obtained prior to starting Mulpleta and no more than two days before the procedure. Patients should undergo their procedure 2-8 days after the last dose of Mulpleta. Mulpleta should be taken orally once daily for 7 consecutive days. Mulpleta has been investigated only as a single 7-day once daily dosing regimen in clinical trials in patients with chronic liver disease. After a 3 mg dose, the median time to reach a maximum platelet count was 12 days and ranged 5-35 days. The median duration of platelet count increase was 20 days. Patients undergoing laparotomy, thoracotomy, open-heart surgery, craniotomy, or organ resection were excluded from the Mulpleta clinical studies. Also patients with a history of splenectomy, partial splenic embolization, or thrombosis and those with Child-Pugh class C liver disease, absence of hepatopetal blood flow, or a prothrombotic condition other than chronic liver disease were not allowed to participate.

Promacta (eltrombopag) is an oral thrombopoietin (TPO) receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy; for the treatment severe aplastic anemia (SAA) who have had an insufficient response to immunosuppressive therapy; and for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy; the safety and efficacy of Promacta (eltrombopag) in combination with direct-acting antiviral agents without interferon have not been established. Promacta is not indicated for the treatment of patients with myelodysplastic syndrome (MDS).



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Tavalisse (fostamatinib) is a tyrosine kinase inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. Tavalisse (fostamatinib) should be discontinued after 12 weeks of treatment if the platelet count does not increase to a level sufficient to avoid clinically important bleeding. Fostamatinib is a phosphate pro-drug that is converted in the gut by alkaline phosphatase into an active metabolite that is a tyrosine kinase inhibitor with demonstrated activity against spleen tyrosine kinase (SYK). The metabolite reduces antibody-mediated destruction of platelets.

TPO is the major physiologic endogenous regulator of platelet production. TPO is made in the liver and it stimulates bone marrow to produce platelets. In CLD, TPO production is reduced, which consequently results in decreased platelet production and increases the likelihood for bleeding and other post-procedure complications.

Thrombocytopenia is one of the most common hematologic disorders, characterized by an abnormally low number of platelets from multiple causes. Thrombocytopenia is defined as a platelet count of less than 150,000 per microliter. A normal count of thrombocytes (or platelets) is between 150,000 and 450,000 per microliter. The clinical expression of thrombocytopenia ranges from asymptomatic to life-threatening bleeding.

Patients with platelet counts greater than 50,000 per microliter rarely have symptoms. A platelet count from 30,000-50,000 per microliter may manifest as purpura. A count from 10,000-30,000 per microliter may cause bleeding with minimal trauma. A platelet count less than 5,000 per microliter may cause spontaneous bleeding and constitutes a hematologic emergency. Various syndromes and diseases are associated with thrombocytopenia.

First-line treatment for thrombocytopenia is usually use of a corticosteroid, such as prednisone or dexamethasone. Intravenous immunoglobulin (IVIG) or intravenous anti-D (Rho[D] immune globulin) can also be used as initial treatment with or without steroids. The most effective second-line treatment option is splenectomy. Other second-line treatment options that may postpone the need of splenectomy include: azathioprine, cyclosporine, cyclophosphamide, danazol, vinca alkaloids, mycophenolate mofetil, rituximab, and thrombopoietin-receptor agonists or other platelet stimulating agents.

ITP is characterized by isolated thrombocytopenia often occurring in the absence of an identifiable cause. It is an autoimmune disorder with immunologic destruction of otherwise normal platelets. ITP has variably been called immune thrombocytopenic purpura, idiopathic thrombocytopenic purpura, and immune thrombocytopenia. ITP is generally considered a benign condition with severe major hemorrhage being rare, bleeding occurs primarily in those with platelet counts  $< 10 \times 10^9/L$ . However bleeding episodes are highly variable; they may range from mild bruising or mucosal bleeding in a generally asymptomatic individual to frank hemorrhage from any site. For ITP, TPO receptor agonists should only be used in patients whose degree of thrombocytopenia and clinical condition increases the risk for major bleeding.

Controlled studies on the treatment of ITP are lacking. The goal of therapy, when needed, is to raise the platelet count high enough to prevent major bleeding. Patients with platelet count of  $\geq 30 \times 10^9/L$  generally do not require

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therapy. Treatment is reserved for patients who are symptomatic or if platelet count is  $< 30 \times 10^9/L$ . General recommendations for first line therapy consists of corticosteroids, intravenous immune globulin, or anti-D immunoglobulin. Splenectomy offers the best chance for cure and is indicated in patients with chronic ITP and platelet counts  $< 30 \times 10^9$  per liter after first line therapy has failed.

Aplastic anemia is a rare, life-threatening disorder of bone marrow failure characterized by pancytopenia and a hypocellular bone marrow. Thrombocytopenia is a major cause of morbidity and mortality in patients with aplastic anemia. The cause of thrombocytopenia is thought to be due to decreased hematopoietic stem and progenitor cell numbers and a reduction in function, resulting in impaired synthesis of megakaryocytes and insufficient mature platelet production. Studies suggest that the ultimate mechanism leading to hematopoietic stem and progenitor depletion is an immune mediated attack and destruction.

Virtually all patients with aplastic anemia have thrombocytopenia. Individuals with platelet counts of  $< 50 \times 10^9/L$  are described as having moderate aplastic anemia while platelet counts of  $< 20 \times 10^9/L$  are considered as having severe aplastic anemia. Bleeding is not typically observed until the platelet count falls below  $10\text{--}20 \times 10^9/L$ . Bleeding events seen in thrombocytopenia of aplastic anemia may consist of petechiae and ecchymoses of the skin and mucous membranes, epistaxis and gingival hemorrhage.

Treatment of thrombocytopenia related to bone marrow failure consists of use of prophylactic platelet transfusions to maintain an adequate number of platelets to avoid significant bleeding, while waiting for a response to immunosuppressive treatment (IST) or allogeneic stem cell transplantation engraftment. Allogeneic bone marrow transplantation offers the best chance for cure in younger patients, but many individuals may not be suitable candidates for transplantation due to advanced age, co-morbidities, or lack of a histocompatible donor. It is estimated that individuals with SAA who are given IST, one-quarter to one-third will not respond, and 30–40% of responders relapse. IST consists of use of the combination of Antithymocyte globulin and Cyclosporine or high dose Cyclophosphamide alone. Corticosteroids may be needed when Antithymocyte globulin is used. Tacrolimus is sometimes used as an alternative for Cyclosporine. There are no standard criteria to judge when IST has failed.

Most guidelines recommend transfusing patients with thrombocytopenia prophylactically when platelets fall to  $< 10 \times 10^9/L$ , or in patients with fevers or a bleeding history with a platelet count of  $< 20 \times 10^9/L$ . However, it is important to realize that the clinical evidence supporting transfusion thresholds remains controversial as these thresholds were primarily derived from patients with hematologic malignancies undergoing chemotherapy or stem cell transplantation, not aplastic anemia.

Thrombocytopenia from use of interferon based hepatic C therapy is well established. As the platelet count falls to below  $50 \times 10^9/L$ , interferon dose reduction is recommended. When the platelet count falls to below  $30 \times 10^9/L$  the recommendation is to discontinue interferon therapy. The mechanism of the thrombocytopenia is thought to include inhibition of proliferation of megakaryocytes, drug induced autoimmune reaction, and impaired TPO production.

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**PHARMACY COVERAGE GUIDELINES**  
**SECTION: DRUGS**

**ORIGINAL EFFECTIVE DATE: 8/02/18**  
**LAST REVIEW DATE: 8/15/19**  
**LAST CRITERIA REVISION DATE: 8/15/19**  
**ARCHIVE DATE:**

**DOPTELET® (avatrombopag) oral tablet**  
**MULPLETA® (lusutrombopag) oral tablet**  
**PROMACTA® (eltrombopag) oral tablet and oral suspension**  
**TAVALISSE™ (fostamatinib) oral tablet**

**Definitions:**

	Route	Treatment of Thrombocytopenia for:			
		CLD Pre-procedures	Chronic ITP	Aplastic anemia	Hep C*
Doptelet (avatrombopag)	Oral	X <sup>†</sup>	X		
Mulpleta (lusutrombopag)	Oral	X <sup>‡</sup>			
Promacta (eltrombopag)	Oral		X	X	X
Tavalisse (fostamatinib)	Oral		X		
Nplate (romiplostim)	SQ injection		X		
CLD: Chronic liver disease ITP: Immune thrombocytopenia Hep C: Hepatitis C  * Used to allow the initiation and maintenance of interferon-based therapy in hepatitis C.  † <b>Doptelet</b> start 10-13 days before the scheduled procedure and then undergo procedure 5-8 days after the last dose. Onset of platelet increase occurs within 3-5 days of the start of treatment with a peak effect after 10-13 days. Median cumulative number of weeks with an increase > 50 x 10 <sup>9</sup> /L is 12.4 weeks (0-25).  ‡ <b>Mulpleta</b> start 8-14 days before the scheduled procedure and then undergo procedure 2-8 days after the last dose. Median time to reach maximum platelet count is 12 days (5-35 days). Median duration of increase to at least 50 x 10 <sup>9</sup> /L 19-22 days (13-28).					

**Resources:**

Mulpleta (lusutrombopag). Package Insert. Revised by manufacturer 7/2018. Accessed 8/23/18.

Doptelet (avatrombopag) product information accessed 07-12-19 at DailyMed

Mulpleta (lusutrombopag) product information accessed 07-12-19 at DailyMed

Promacta (eltrombopag) product information accessed 07-13-19 at DailyMed

Tavalisse (fostamatinib) product information accessed 07-13-19 at DailyMed

UpToDate: Immune thrombocytopenia (ITP) in adults: Initial management and prognosis. Current through Jun 2018



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UpToDate: Immune thrombocytopenia ITP in adults: Second line and subsequent therapies. Current through Jun 2018

UpToDate: Extrahepatic manifestations of hepatitis C virus infection. Current through Jun 2018

UpToDate: Approach to the adult with unexplained thrombocytopenia. Current through Jun 2018

UpToDate: Clinical and laboratory aspects of platelet transfusion therapy. Current through Jun 2018

DeZern AE, Brodsky RA.: Clinical management of aplastic anemia. Expert Rev Hematol 2011 April; 4(2): 221-230 NIH Public Access.

Lin KH, Hsu PI, Yu HC, et al.: Factors related to severe thrombocytopenia during antiviral therapy in patients with chronic hepatitis c and pretreatment low platelet counts. BMC Gastroenterol 2012, 12:7.

Kuter DL: The biology of thrombopoietin and thrombopoietin receptor agonists. In J Hematol 2013 98: 10-23.

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