avatrombopag (Doptelet®), eltrombopag (Promacta®), lusutrombopag (Mulpleta®), fostamatinib (Tavalisse™) EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO169

Description

Avatrombopag (Doptelet ®), eltrombopag (Promacta ®), lusutrombopag (Mulpleta ®) are thrombopoietin (TPO) receptor agonists that induce the proliferation and differentiation of megakaryocytic progenitor cells from hematopoietic stem cells and megakaryocyte maturation, thus resulting in an increased production of platelets.

Fostamatinib (Tavalisse™) is a tyrosine kinase inhibitor (TKI) with activity against spleen tyrosine kinase (SYK). Fostamatinib metabolite, R406, inhibits signal transduction of Fc-activating receptors, B-cell receptors, and reduces antibody-mediated destruction of platelets.

Length of Authorization

- Initial:
  - **Avatrombopag (Doptelet)**
    - Thrombocytopenia associated with chronic liver disease, prior to planned procedure: one month
    - Chronic immune thrombocytopenia (ITP): Three months
  - **Eltrombopag (Promacta)**
    - Chronic thrombocytopenia due to chronic hepatitis C: three months
    - Chronic Immune Thrombocytopenia (ITP): three months
    - First-line treatment severe aplastic anemia: six months
    - Severe aplastic anemia, refractory: four months
  - **Lusutrombopag (Mulpleta)**
    - Thrombocytopenia associated with chronic liver disease, prior to planned procedure: one month
  - **Fostamatinib (Tavalisse)**
    - Chronic Immune Thrombocytopenia (ITP): three months

- Renewal:
  - **i. Avatrombopag (Doptelet), eltrombopag (Promacta) and fostamatinib (Tavalisse)**
    - Chronic Immune Thrombocytopenia (ITP), refractory severe aplastic anemia, chronic thrombocytopenia due to chronic hepatitis C: six months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
avatrombopag (Doptelet)	20 mg tablet	Thrombocytopenia associated with chronic liver disease, prior to planned procedure	15 tablets/ 30 days
		Chronic Immune Thrombocytopenia (ITP)	60 tablets/30 days
eltrombopag (Promacta)	12.5 mg/1 packet	Severe aplastic anemia	***[2 to 5 Years of age]*** 2.5mg/kg/day ***[6 to 11 Years of age]*** 180 packets/30 days (6 kits/30 days) ***[12 years and older]*** 360 packets/30 days (12 kits/30 days)
	12.5 mg tablet		30 tablets/ 30 days
	25 mg tablet		30 tablets/ 30 days
	50 mg tablet		30 tablets/ 30 days
	75 mg tablet		60 tablets/ 30 days
	12.5 mg/1 packet	Chronic thrombocytopenia due to chronic Hepatitis C	240 packets/ 30 days (8 kits/30 days)
	12.5 mg tablet		30 tablets/ 30 days
	25 mg tablet		30 tablets/ 30 days
	50 mg tablet		60 tablets/ 30 days
	75 mg tablet		30 tablets/ 30 days
	12.5 mg/1 packet	Chronic immune thrombocytopenia (ITP)	180 packets/30 days (6 kits/30 days)
	12.5 mg tablet		30 tablets/ 30 days
	25 mg tablet		
	50 mg tablet		
	75 mg tablet		
lusutrombopag (Mulpleta)	3 mg tablet	Thrombocytopenia associated with chronic liver disease, prior to planned procedure	7 tablets/ 365 days
fostamatinib (Tavalisse)	100 mg tablets	Chronic Immune Thrombocytopenia	60 tablets/30 days
	150 mg tablets		

Initial Evaluation

I. Avatrombopag (Doptelet), eltrombopag (Promacta), lusutrombopag (Mulpleta) and fostamatinib (Tavalisse) may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, a hematologist or gastroenterologist; **AND**
   B. Medication is not used in combination with another thrombopoietin (TPO) receptor agonists (e.g. avatrombopag, eltrombopag, lusutrombopag); **AND**
   C. A diagnosis of one of the following:
      1. **Chronic liver disease (CLD)-associated thrombocytopenia**; **AND**
         i. Member is 18 years of age or older; **AND**
         ii. Documentation of platelet count less than 50 x 10^9/L; **AND**
         iii. Request is for *avatrombopag (Doptelet) OR lusutrombopag (Mulpleta);* **AND**
            a. Member is scheduled to undergo an invasive procedure that carries an intermediate-to-high risk of bleeding (e.g. spinal surgery, cardiac surgery, large polypectomy, or liver biopsy); **OR**
         iv. Member has a documented diagnosis of **chronic Hepatitis C** infection; **AND**
            a. Member is unable to initiate or maintain interferon-based treatment [eg. pegylated interferon (Pegasys®) and ribavirin]; **AND**
            b. Request is for *eltrombopag (Promacta)* tablet formulation; **OR**
            c. Request is for *eltrombopag (Promacta)* packets; **AND**
               1. Member is unable to swallow tablets; **OR**
      2. **Chronic Immune Thrombocytopenia; AND**
         i. Treatment with first-line therapies (e.g corticosteroids, immunoglobulins, or splenectomy) have been ineffective, contraindicated, or not tolerated; **AND**
         ii. Documentation of platelet count that is less than 30 x 10^9/L with symptoms of bleeding; **AND**
         iii. Member is one year of age or older; **AND**
            a. Request is for *eltrombopag (Promacta)* tablet formulation; **OR**
            b. Request is for *eltrombopag (Promacta)* packets; **AND**
               1. Member is unable to swallow tablets; **OR**
         iv. Member is 18 years of age or older; **AND**
            a. Request is for *avatrombopag (Doptelet)*; **OR**
            b. Request is for *fostamatinib (Tavalisse);* **OR**
      3. **Severe aplastic anemia; AND**
         i. Member has met at least two of the following three criteria:
            1. Absolute neutrophil count (ANC) less than 500/microL; **OR**

2. Platelet count less than 20,000/microL; **OR**
3. Absolute reticulocyte count (ARC) less than 60,000/microL; **AND**

ii. Member has NOT received prior immunosuppressive therapy (IST); **AND**
   a. Member is two years of age or older; **AND**
   b. Eltrombopag (Promacta) will be initiated concurrently with immunosuppressive therapy (e.g., horse antithymocyte globulin (h-ATG) and cyclosporine); **OR**

iii. Member has severe aplastic anemia with refractory thrombocytopenia; **AND**
   a. Treatment with at least one course of horse or rabbit anti-thymocyte globulin (ATG) and cyclosporine A (CSA) has been ineffective, contraindicated or not tolerated; **AND**

iv. Request is for *eltrombopag (Promacta)* tablet formulation; **OR**

v. Request is for *eltrombopag (Promacta)* packets; **AND**
   a. Member is unable to swallow tablets

II. Avatrombopag (Doptelet) is considered investigational when used for all other conditions, including but not limited to:
   A. Chemotherapy-induced thrombocytopenia in adults with active non-hematological cancers

III. Eltrombopag (Promacta) is considered investigational when used for all other conditions, including but not limited to:
   A. Elderly patients with Acute Myeloid Leukemia receiving induction chemotherapy
   B. Prevention of chemotherapy induced thrombocytopenia
   C. Thrombocytopenia with chronic HBV infection
   D. Thrombocytopenia after consolidation therapy in acute myeloid leukemia (AML)
   E. Thrombocytopenia associated with myelodysplastic syndrome

IV. Lusutrombopag (Mulpleta) is considered investigational when used for all other conditions.

V. Fostamatinib (Tavalisse) is considered investigational when used for all other conditions, including but not limited to:
   A. Malignancies:
      1. Advanced colorectal, non-small cell lung, head and neck hepatocellular and renal cell carcinomas, and pheochromocytoma and thyroid tumors
      2. B-cell Lymphoma
      3. Large B-Cell Lymphoma
      4. Ovarian Cancer
      5. T-Cell Lymphoma
   B. Rheumatoid Arthritis (RA)

C. Renal Transplant Rejection (antibody mediated rejection)
D. Chronic Graft vs. Host Disease

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms; **AND**
   A. **Chronic thrombocytopenia due to chronic Hepatitis C**; **AND**
      1. Member is unable to initiate or maintain interferon-based treatment [e.g. pegylated interferon (Pegasys®) and ribavirin]; **OR**
   B. **Chronic Immune Thrombocytopenia**; **AND**
      1. Platelet count has increased to greater than or equal to 50 x10^9/L; **OR**
   C. **Severe aplastic anemia; AND**
      1. Absolute neutrophil count (ANC) less than 500/microL at baseline; **AND**
         i. ANC has increased 100%; **OR**
         ii. An ANC increase greater than or equal to 500/microL; **OR**
      2. Platelet count was less than 20,000/microL at baseline; **AND**
         i. Increase in platelet count has been greater than or equal to 20,000/microL from baseline; **OR**
         ii. Stable platelet counts with transfusion independence for ≥ 8 weeks; **OR**
      3. Absolute reticulocyte count (ARC) less than 60,000/microL at baseline; **AND**
         i. There has been an increase in hemoglobin by 1.5 g/dL; **OR**
         ii. In patients receiving transfusions, there has been a reduction in red blood cell transfusions.

Supporting Evidence

I. The clinical trials for avatrombopag (Doptelet), eltrombopag (Promacta), lusutrombopag (Mulpleta), and fostamatinib (Tavalisse) did not include patients who were concomitantly using another TPO receptor agonists. Due to this, there is no data to assess the safety and efficacy of these agents when used concomitantly.
II. Considering the complexity of the indications and agents, they must be prescribed by, or in consultation with, a hematologist or gastroenterologist.

III. The safety and efficacy clinical trials of avatrombopag (Doptelet), eltrombopag (Promacta), and lusutrombopag (Mulpleta) for chronic liver disease (CLD)-associated thrombocytopenia, did not include patients younger than 18 years of age. Therefore, there is no clinical trial data to support the use of these agents in pediatric patients.

IV. Avatrombopag (Doptelet), eltrombopag (Promacta), and lusutrombopag (Mulpleta), for chronic liver disease (CLD)-associated thrombocytopenia, were studied in patients with a platelet count less than 50 x 10^9/L. This is because the risk for serious bleeding does not occur until the platelet count becomes very low–less than 10 x 10^9/L or 20 x 10^9/L, with the risk for mild bleeding occurring when the platelet count is less than 50 x 10^9/L. These agents should not be administered to patients with chronic liver disease, without associated thrombocytopenia or risk of surgical bleed, in an effort to normalize platelet counts (normal platelet count in adults ranges from 150 x 10^9/L to 450 x 10^9/L).

V. Avatrombopag (Doptelet) and lusutrombopag (Mulpleta) are indicated for the treatment of thrombocytopenia in adults with chronic liver disease who are scheduled to undergo a procedure that carries an intermediate-to-high risk of bleeding (e.g. spinal surgery, cardiac surgery, large polypectomy, liver biopsy). They should not be administered to patients with chronic liver disease, without associated thrombocytopenia or risk of surgical bleed, in an effort to normalize platelet counts (normal platelet count in adults ranges from 150 x 10^9/L to 450 x 10^9/L).

VI. Eltrombopag (Promacta) is indicated for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. It 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. It should not be used to normalize platelet counts outside of this indication (normal platelet count in adults ranges from 150 x 10^9/L to 450 x 10^9/L).

VII. There is no safety and efficacy data to show superiority of one formulation over the other.

VIII. Avatrombopag (Doptelet), eltrombopag (Promacta), and fostamatinib (Tavalisse) are indicated for the treatment of patients with chronic immune thrombocytopenia who have had an insufficient response to a first-line treatment (e.g. corticosteroids, immunoglobulins, or splenectomy).

IX. Patients with platelet counts less than 30 x 10^9/L were included in clinical trials for avatrombopag (Doptelet), eltrombopag (Promacta), and fostamatinib (Tavalisse).

X. The efficacy and safety of eltrombopag (Promacta) in pediatric patients one year and older with chronic ITP were evaluated in two double-blind, placebo-controlled trials. The trials differed in time since ITP diagnosis: at least 6 months versus at least 12 months. The primary endpoint was participants who achieved a platelet count greater than, or equal to, 50 x 10^9/L for at least six out of eight weeks, generally seen between weeks five and 12. Pediatric patients (75%) treated with eltrombopag (Promacta), compared with placebo (21%), saw an increased value with at least one platelet count greater than, or equal to, 50 x 10^9/L during the first 12 weeks of

randomized treatment in absence of rescue therapy. Platelet response to eltrombopag (Promacta) was consistent across the age cohorts. Fewer pediatric patients treated required rescue treatment during the randomized, double blind period compared with placebo-treated patients (13% [6/45] versus 50% [11/22]).

XI. The safety and efficacy clinical trials of avatrombopag (Doptelet) and fostamatinib (Tavalisse), for chronic ITP, did not include patients younger than 18 years of age.
    - Fostamatinib (Tavalisse) is not recommended for use in patients less than 18 years of age because adverse effects on actively growing bones were observed in nonclinical studies. In subchronic, chronic, and carcinogenicity studies, chondrodystrophy of the femoral head was seen in rodents.

XII. Eltrombopag (Promacta) is indicated in combination with standard immunosuppressive therapy for the first-line treatment of severe aplastic anemia and of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.

XIII. According to aplastic anemia & MDS international foundation (AAMDS) for a confirmed diagnosis of aplastic anemia the patient has to have met at least two of the following cell counts: absolute neutrophil count (ANC) less than 500/microL, platelet count less than 20,000/microL, or absolute reticulocyte count (ARC) less than 60,000/microL.

XIV. Thirty-four patients, two to 16 years of age, were enrolled in Study US01T. The primary outcome was rate of complete hematologic response at six months. In the D1-M6 cohort, 7 and 17 out of 25 pediatric patients achieved a complete and overall response, respectively, at six months.

XV. Ninety-two patients were enrolled in a prospective phase 1-2 study of immunosuppressive therapy plus eltrombopag. The three consecutively enrolled cohorts differed regarding the timing of initiation and the duration of the eltrombopag regimen (cohort 1 received eltrombopag from day 14 to six months, cohort 2 from day 14 to three months, and cohort 3 from day one to six months). The primary outcome was complete hematologic response at 6 months. Secondary end points included overall response, survival, relapse, and clonal evolution to myeloid cancer. The rate of complete response at 6 months was 33% in cohort 1, 26% in cohort 2, and 58% in cohort 3. The overall response rates at 6 months was 80% cohort 1, 87% cohort 2, and 94% cohort 3. The addition of eltrombopag to immunosuppressive therapy (e.g. horse antithymocyte globulin (h-ATG) and cyclosporine) was associated with higher rates of hematologic response among patients with severe aplastic anemia than in a historical cohort.

XVI. Eltrombopag (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.

XVII. Eltrombopag (Promacta) is indicated for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. It 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. It should not be used to normalize platelet counts.(normal platelet count in adults ranges from 150 x 10^9/L to 450 x 10^9/L).

XVIII. Treatment with avatrombopag (Doptelet), eltrombopag (Promacta), and fostamatinib (Tavalisse) should be discontinued after 12 weeks (three months) of treatment if platelet counts do not increase to a level sufficient to avoid clinically important bleeding (greater than or equal to 50 x10^9 /L – risk for serious bleeding doesn't occur until the count becomes very low—less than 10 x 10^9/L or 20 x 10^9/L, and for mild bleeding when the count is less than 50 x 10^9/L). These agents should not be administered to patients with chronic liver disease, that do not meet this criterion, in an effort to normalize platelet counts (normal platelet count in adults ranges from 150 x 10^9/L to 450 x 10^9/L).

XIX. In the clinical trial, the primary end point was hematologic response at three to four months and defined as uni- or multilineage recovery by one or more of the following criteria: (1) platelet response (increase to 20 × 10^3/µL above baseline or stable platelet counts with transfusion independence for a minimum of 8 weeks in those who were transfusion dependent on entry into the protocol); (2) erythroid response (when pretreatment hemoglobin was <9 g/dL, defined as an increase in hemoglobin by 1.5 g/dL or, in transfused patients, a reduction in the units of packed red blood cell transfusions by an absolute number of at least 4 transfusions for 8 consecutive weeks, compared with the pretreatment transfusion number in the previous 8 weeks); and (3) neutrophil response (when pretreatment absolute neutrophil count [ANC] of <0.5 × 10^3/µL as at least a 100% increase in ANC, or an ANC increase >0.5 × 10^3/µL, and the toxicity profile as measured using Common Terminology Criteria for Adverse Events).

Investigational or Not Medically Necessary Uses

I. Avatrombopag (Doptelet)
   A. Chemotherapy-Induced Thrombocytopenia in adults with active non-hematological cancers
      i. A randomized, double-blind, placebo-controlled study with an open-label extension to evaluate the efficacy and safety of avatrombopag (Doptelet) for the treatment of chemotherapy-induced thrombocytopenia in subjects with active non-hematological cancers is still recruiting.
   B. There is limited or no published clinical trial data to support the use of avatrombopag (Doptelet) in conditions other than thrombocytopenia associated with chronic liver disease prior to planned procedure and chronic immune thrombocytopenia (ITP).

II. Eltrombopag (Promacta)
   A. Elderly Patients with Acute Myeloid Leukemia receiving induction chemotherapy (EPAG2015)
      i. A Phase II, randomized, placebo-controlled study to assess the impact on outcome of eltrombopag (Promacta) administered to elderly patients with acute myeloid

leukemia receiving induction chemotherapy in 110 participants and is still recruiting.

B. Prevention of chemotherapy induced thrombocytopenia
    i. A phase I/II open-label study of eltrombopag for the prevention of chemotherapy induced thrombocytopenia (CIT) in subjects with advanced soft tissue and bone sarcomas receiving gemcitabine and docetaxel chemotherapy was terminated.
C. Thrombocytopenia with chronic HBV infection
    i. A multicenter, single-arm, open-label study in 58 participants to evaluate the efficacy and safety of eltrombopag for thrombocytopenia in Chinese patients with chronic HBV infection is still recruiting.
D. Thrombocytopenia after consolidation therapy in acute myeloid leukemia (AML)
    i. Randomized, single arm, single-blind study in 220 participants of eltrombopag (Promacta) in thrombocytopenia after consolidation therapy in acute myeloid leukemia (AML) is in recruiting stage.
E. Thrombocytopenia associated with myelodysplastic syndrome
    i. In a three-part study of eltrombopag in thrombocytopenic subjects with myelodysplastic syndromes or acute myeloid leukemia.
        1. Part 1 was an open-label with 17 patients receiving eltrombopag and 11 patients completing treatment. Primary endpoint was number of participants with platelet response up to week 8 and four experienced significantly increased platelet counts, and ten had reduced platelet transfusion requirements.
        2. Part 2 was a randomized, double-blind with 145 patients who received supportive care plus eltrombopag (n=98) or placebo (n=47). Primary outcome was clinically relevant thrombocytopenic events (CRTE) from week 5 up to week 12. Average weekly CRTE were significantly lower with eltrombopag (54% [95% CI 43-64]) than with placebo (69% [57-80], odds ratio [OR] 0·20, 95% CI 0·05-0·87; p=0·032) although the difference between treatment groups was less than 30%. Serious adverse events were reported in 56 (58%) eltrombopag-treated patients and 32 (68%) placebo-treated patients. Seven eltrombopag recipients and two placebo recipients had serious adverse events that were suspected to be study drug-related (acute kidney injury, arterial thrombosis, bone pain, diarrhea, myocardial infarction, pyrexia, retinal vein occlusion, n=1 each; placebo: vomiting, white blood cell count increased, n=1 each). Two eltrombopag recipients had arterial thrombosis n=1 and myocardial infarction n=1. No placebo recipients experienced fatal or serious adverse events suspected to be study drug related.
        3. Part 3 is an extension ongoing study.

4. Overall the clinical trial had a small patient population, showed limited efficacy and had questionable safety.

ii. Safety and tolerability of eltrombopag versus placebo for treatment of thrombocytopenia in patients with advanced myelodysplastic syndromes or acute myeloid leukemia was completed in a multicenter, randomized, placebo-controlled, double-blind, phase 1/2 trial.

1. Primary outcome was safety and tolerability parameters including non-hematological laboratory Grade 3/Grade 4 toxicities, change in bone marrow blast counts from baseline, and adverse events reporting. [Time Frame: Approximately 46 months].
2. Ninety-eight patients were randomized to receive either eltrombopag (n=64) or placebo (n=34). Sixty-three (98%) patients in the eltrombopag group and 32 (94%) patients in the placebo group had adverse events. The most common adverse events were pyrexia (27 [42%] vs 11 [32%]), nausea (20 [31%] vs 7 [21%]), diarrhea (19 [30%] vs 6 [18%]), fatigue (16 [25%] vs 6 [18%]), decreased appetite (15 [23%] vs 5 [15%]), and pneumonia (14 [22%] vs 8 [24%]). Drug-related adverse events of grade 3 or higher were reported in six (9%) patients in the eltrombopag group and four (12%) patients in the placebo group.
3. In this clinical trial efficacy was not assessed.

F. There is limited or no published clinical trial data to support the use of eltrombopag (Promacta) in conditions other than severe aplastic anemia, chronic thrombocytopenia due to chronic hepatitis C, and chronic immune thrombocytopenia (ITP).

III. Lusutrombopag (Mulpleta)

A. There is limited or no published clinical trial data to support the use of lusutrombopag (Mulpleta) in conditions other than thrombocytopenia associated with chronic liver disease prior to a planned procedure.

IV. Fostamatinib (Tavalisse)

A. Malignancies

i. Advanced colorectal, non-small cell lung, head, and neck, hepatocellular and renal cell carcinomas, pheochromocytoma, and thyroid tumors

1. A broad, multi-histology, single group assignment, open label, phase II study of the multi-kinase inhibitor R935788 (fostamatinib disodium) in advanced colorectal, non-small cell lung, head and neck, hepatocellular and renal cell carcinomas, pheochromocytoma, and thyroid tumors in in 37 participants.
2. Fostamatinib had limited anti-tumor activity in this first clinical trial in patients with advanced refractory solid tumors; reduction in CECs and

CEPs was indicative of anti-angiogenic effects. Abnormal liver testing at baseline appeared to influence drug tolerability.

B. B-cell Lymphoma
    i. A Phase I/II, multi-Center, single group assignment, open label trial of the safety and efficacy of fostamatinib in 81 patients with relapsed/refractory B-cell lymphoma. The clinical trial showed limited efficacy and considering it is an open label, single group trial, further clinical research is necessary to show efficacy and safety.
C. Large B-cell lymphoma, relapsed or refractory
    i. Phase II, single group assignment, open label trial with 101 participants to evaluate the efficacy of fostamatinib in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). The clinical trial showed limited efficacy and considering it is an open label, single group trial, further clinical research is necessary to show efficacy and safety.
D. Ovarian cancer
    i. Phase I, single group assignment, open label clinical trial of combined fostamatinib and paclitaxel in ovarian cancer with 18 participants and still recruiting.
E. T-cell lymphoma
    i. Phase II, multicenter, open label, single assessment group, simon two-stage study of fostamatinib disodium in patients with relapsed or refractory T-cell lymphoma in 18 participants. The clinical trial was not blinded or randomized. It wasn't powered enough to show efficacy or safety of fostamatinib (Tavalisse) in T-cell lymphoma.
F. Rheumatoid arthritis (RA)
    i. A Long-term, open label, single assignment study to assess the safety of fostamatinib in the treatment of rheumatoid arthritis in Asia was terminated.
    ii. A Phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study of two dosing regimens of fostamatinib in patients with rheumatoid arthritis with an inadequate response to a tumor necrosis factor-α antagonist.
    - Adult patients were randomized (1:1:1) to fostamatinib [100 mg bid for 24 weeks (n=105; Group A)], or 100 mg bid for 4 weeks, then 150 mg qd (n=108; Group B), or to placebo (n=110; Group C) for 24 weeks. Nonresponders at Week 12 could enter a long-term extension study. The primary endpoint was the proportion of patients achieving an American College of Rheumatology 20% (ACR20) response at Week 24.
    - Due to efficacy and safety results from the clinical trial, the companies developing fostamatinib have decided not to study it further in RA at this time.
G. Renal Transplant Rejection (antibody mediated rejection)
    i. Fostamatinib is being studied in a phase 2, single center, not randomized, open label, pilot study to assess the safety and efficacy of fostamatinib in the treatment

of chronic active antibody mediated rejection in renal transplantation is still recruiting.

H. Chronic Graft vs. Host Disease
    i. A phase I, open label, single group assignment trial of fostamatinib and chronic graft vs. host disease development after allogeneic stem cell transplantation with 18 participants is still recruiting.

I. There is limited or no published clinical trial data to support the use of fostamatinib (Tavalisse) in conditions other than chronic immune thrombocytopenia (ITP).

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Policy Implementation/Update:

Action and Summary of Changes	Date
• Added investigational indications for avatrombopag (Doptelet), eltrombopag (Promacta), lusutrombopag (Mulpleta) • Added age limits to eltrombopag (Promacta) for immunosuppressive naive Severe aplastic anemia at two years of age or older, and relapsed or refractory severe aplastic anemia at 18 years of age or older. • Added criteria for Severe aplastic anemia; [Member has to meet at least two of the following three criteria are met: 1) Absolute neutrophil count (ANC) less than 500/microL, or 2) Platelet count less than 20,000/microL, or 3) Absolute reticulocyte count (ARC) less than 60,000/microL • Added member is 18 years of age or older if request is for avatrombopag (Doptelet), fostamatinib (Tavalisse) and fostamatinib (Tavalisse) [for chronic ITP] • Added criteria if request is for eltrombopag (Promacta) packets, member has demonstrated inability to swallow tablets • Changed QL for eltrombopag (Promacta) packets • Changed QL for avatrombopag (Doptelet) for chronic immune thrombocytopenia (ITP) • Changed initial and renewal length of authorization for all agents • Combined as one policy: avatrombopag (Doptelet), eltrombopag (Promacta), lusutrombopag (Mulpleta) with fostamatinib (Tavalisse)	02/2020
Previous reviews fostamatinib (Tavalisse)	06/2018, 11/2019,
Conversion to policy format fostamatinib (Tavalisse)	11/2019
Avatrombopag (Doptelet), eltrombopag (Promacta), lusutrombopag (Mulpleta) combined as policy: TPO-Receptor Agonists	10/2019
Previous reviews avatrombopag (Doptelet), eltrombopag (Promacta), lusutrombopag (Mulpleta)	10/2019,
Policy created avatrombopag (Doptelet), eltrombopag (Promacta), lusutrombopag (Mulpleta)	10/2019
Policy created fostamatinib (Tavalisse)	06/2018