BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 8/02/18**
SECTION: DRUGS	**LAST REVIEW DATE: 9/20/18**
	LAST CRITERIA REVISION DATE: 9/20/18
	ARCHIVE DATE:

DOPTELET® (avatrombopag) oral tablet
MULPLETA® (lusutrombopag) oral tablet

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.

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.

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.

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. **Incomplete forms or forms without the chart notes will be returned.**

DOPTELET® (avatrombopag) oral tablet
MULPLETA® (lusutrombopag) oral tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Doptelet (avatrombopag) and Mulpleta (lusutrombopag) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual is 18 years of age or older

2. A confirmed diagnosis of thrombocytopenia in an individual with chronic liver disease scheduled to undergo an elective procedure

3. Individual has failure, contraindication or intolerance to **BOTH** the following preferred step therapy agents:
   - Dexamethasone
   - Methylprednisolone

4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
   - **For Doptelet:** Platelet count prior to administration and on the day of the procedure
   - **For Mulpleta:** Platelet count prior to administration and no more than 2 days before the procedure
   - Baseline platelet count prior to use of Doptelet is $< 50 \times 10^9$/L
   - Basic metabolic panel

5. Will not be used in an attempt to normalize platelet count

6. **ONE** of the following:
   - **Doptelet** will not be used in neurosurgical interventions, thoracotomy, laparotomy, or organ resection
   - **Mulpleta** will not be used in patients undergoing thoracotomy, laparotomy, organ resection, open-heart surgery, or craniotomy, history of splenectomy, partial splenic embolization, or thrombosis, patients with Child Pugh Class-C, absence of hepatopetal blood flow, or a prothrombotic condition other than liver disease

7. Will not be used with a thrombopoietic agent or Spleen Tyrosine Kinase Inhibitor e.g., Promacta (eltrombopag), Nplate (romiplostim), or Tavalisse (fotamatinib)

8. Will not be used in severe renal impairment (creatinine clearance < 30 mL/min by Cockroft-Gault), including patients who require hemodialysis

Initial approval duration:
For Doptelet: 5 day supply per procedure, no refills will be allowed
For Mulpleta: 7 day supply per procedure, no refills will be allowed

DOPTELET® (avatrombopag) oral tablet
MULPLETA® (lusutrombopag) oral tablet (cont.)

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 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.

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 to 50,000 per microliter may manifests as purpura. A count from 10,000 to 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.

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MULPLETA® (lusutrombopag) oral tablet (cont.)

First-line treatment 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.

Definitions:

Doptelet Recommended Dose and Duration:

Platelet Count (x10^9/L)	Once Daily Dose	Duration
< 40	60 mg (3 tablets)	5 days
40 to < 50	40 mg (2 tablets)	5 days

Resources:

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

Doptelet (avatrombopag) product information accessed 07-11-2018 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=e2d5960d-6c18-46cc-86bd-089222b09852

UpToDate: Immune thrombocytopenia (ITP) in adults: Initial management and prognosis. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/immune-thrombocytopenia-itp-in-adults-initial-treatment-and-prognosis?topicRef=6676&source=see_link

UpToDate: Immune thrombocytopenia (ITP in adults: Second line and subsequent therapies. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/immune-thrombocytopenia-itp-in-adults-second-line-and-subsequent-therapies?topicRef=6676&source=see_link

UpToDate: Extrahepatic manifestations of hepatitis C virus infection. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/extrahepatic-manifestations-of-hepatitis-c-virus-infection?sectionName=Immune%20thrombocytopenia%20(ITP)%20and%20autoimmune%20hemolytic%20anemia&topicRef=6677&anchor=H11&source=see_link#H11

UpToDate: Approach to the adult with unexplained thrombocytopenia. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/approach-to-the-adult-with-unexplained-thrombocytopenia?search=thrombocytopenia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

UpToDate: Clinical and laboratory aspects of platelet transfusion therapy. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-and-laboratory-aspects-of-platelet-transfusion-therapy?search=thrombocytopenia%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.