Doptelet® (avatrombopag)
(Oral)

Document Number: IC-0369

Last Review Date: 02/04/2020
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Dates Reviewed: 07/2018, 02/2019, 08/2019, 02/2020

I. Length of Authorization

Thrombocytopenia due to CLD
- Coverage is provided for one 5-day course of therapy and may not be renewed.

Chronic ITP
- Coverage is provided for three months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC unit]:
- 20 mg tablets: 3 tablets per day

B. Max Units (per dose and over time) [HCPCS Unit]:

Thrombocytopenia
- 60 mg daily

Chronic ITP
- 40 mg daily

III. Initial Approval Criteria[1]

Coverage is provided in the following conditions:

Universal Criteria

- Patient age 18 years or older; **AND**
- Patient is not on any other thrombopoietin receptor agonist or mimetic (e.g., romiplostim, eltrombopag, lusutrombopag, etc.) or fostamtinib; **AND**
- Avatrombopag is not being used to attempt to normalize platelet count; **AND**
- Laboratory values are current (i.e., drawn within the previous 28 days); **AND**

Thrombocytopenia due to Chronic Liver Disease (CLD) †

- Patient is scheduled to undergo a procedure with a risk of bleeding which would necessitate a platelet transfusion; **AND**
- Patient will not be undergoing any of the following procedures:
  - Neurosurgical intervention;
  - Thoracotomy;
  - Laparotomy;
  - Organ resection; **AND**
- The patient is at increased risk for bleeding as indicated by platelet count of less than < 50 x 10^9/L

Chronic Immune Thrombocytopenia (ITP) †

- Patient has had chronic ITP for at least 6 months (or meets the corticosteroid requirement below); **AND**
- Patient has previously failed any of the following treatments for ITP:
  - Patient has failed previous therapy with corticosteroids (i.e., patient had no response to at least a 3-month trial or is corticosteroid-dependent); **OR**
  - Patient has failed previous therapy with immunoglobulins; **OR**
  - Patient has had splenectomy; **AND**
- The patient is at increased risk for bleeding as indicated by platelet count of less than 30 × 10^9/L (30,000/mm^3)

† FDA Approved Indication(s)

IV. Renewal Criteria[1]

Coverage can be renewed based upon the following criteria:

Chronic ITP

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: thrombotic/thromboembolic complications (blood clots), etc.; **AND**
- Platelet count (within the preceding 28 days) does not exceed 400 x 10^9/L; **AND**
- Disease response indicated by the achievement and maintenance of a platelet count of at least 50 × 10^9/L as necessary to reduce the risk for bleeding

Thrombocytopenia due to CLD

- Coverage CANNOT be renewed.

V. Dosage/Administration[1]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Thrombocytopenia secondary to CLD</td><td>

Begin Doptelet 10-13 days prior to scheduled procedure.
Patients should undergo their procedure within 5-8 days after the last dose.

Take Doptelet once daily, with food, for 5 consecutive days (dose is based on platelet count.
<table>
<tr><th>Platelet Count (x10^9/L)</th><th>Once Daily Dose</th><th>Duration</th></tr>
<tr><td>Less than 40</td><td>60 mg (3 tablets)</td><td>5 days</td></tr>
<tr><td>40 to less than 50</td><td>40 mg (2 tablets)</td><td>5 days</td></tr>
</table>
</td></tr>
<tr><td>Chronic ITP</td><td>

Initial Dose Regimen: Begin Doptelet at a starting dose of 20 mg (1 tablet) once daily with food.

Monitoring: After initiating therapy, assess platelet counts weekly until a stable platelet count ≥ 50 x10^9/L has been achieved, and then obtain platelet counts monthly thereafter. Obtain platelet counts weekly for at least 4 weeks following discontinuation of therapy.

Dose Adjustments: Based on platelet count response.

<table>
<tr><th>Platelet Count (x10^9/L)</th><th>Dose Adjustment or Action</th></tr>
<tr><td>< 50 after at least 2 weeks of therapy</td><td>• Increase One Dose Level per table below.
• Wait 2 weeks to assess the effects of this regimen and any subsequent dose adjustments.</td></tr>
<tr><td>Between 200 and 400</td><td>• Decrease One Dose Level per table below.
• Wait 2 weeks to assess the effects of this regimen and any subsequent dose adjustments.</td></tr>
<tr><td>Greater than 400</td><td>• Stop Doptelet.
• Increase platelet monitoring to twice weekly.
• When platelet count is less than 150 x10^9/L, decrease One Dose Level per table below and reinitiate therapy.</td></tr>
<tr><td>< 50 after 4 weeks of Therapy at 40 mg once daily</td><td>• Discontinue DOPTELET.</td></tr>
<tr><td>> 400 after 2 weeks of therapy at 20 mg weekly</td><td>• Discontinue DOPTELET.</td></tr>
</table>

Dose Level Titration Table

<table>
<tr><th>Dose</th><th>Dose Level</th></tr>
<tr><td>40 mg once daily</td><td>6</td></tr>
<tr><td>40 mg three times weekly AND 20 mg on the four remaining days of each week</td><td>5</td></tr>
<tr><td>20 mg once daily*</td><td>4</td></tr>
<tr><td>20 mg three times weekly</td><td>3</td></tr>
<tr><td>20 mg twice weekly OR 40 mg once weekly</td><td>2</td></tr>
<tr><td>20 mg once weekly</td><td>1</td></tr>
<tr><td colspan="2">*Initial dose regimen for all patients except those taking Moderate or Strong Dual Inducers or Moderate or Strong Dual Inhibitors of CYP2C9 and CYP3A4.</td></tr>
</table>
</td></tr>
</table>

VI. Billing Code/Availability Information

HCPCS code:

- J8499 – Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified
- C9399 – Unclassified drugs or biologicals (Hospital Outpatient Use ONLY)

NDC:

- Doptelet 20 mg tablets in blister-cards: 71369-0020-xx

VII. References

1. Doptelet [package insert]. Durham, NC; AkaRx, Inc; June 2019. Accessed January 2020.
2. American Society of Anesthesiologists Task Force on Perioperative Blood Management. Practice guidelines for perioperative blood management: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management*.Anesthesiology. 2015 Feb;122(2):241-75.
3. Argo CK, Balogun RA. Blood products, volume control, and renal support in the coagulopathy of liver disease. Clin Liver Dis. 2009;13(1):73.
4. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019 Dec 10;3(23):3829-3866.
5. Jurczak W, Chojnowski K, Mayer J, et al. Phase 3 randomised study of avatrombopag, a novel thrombopoietin receptor agonist for the treatment of chronic immune thrombocytopenia. Br J Haematol. 2018;183(3):479-490. doi: 10.1111/bjh.15573.
6. Terrault N, Chen YC, Izumi N, et al. Avatrombopag before procedures reduces need for platelet transfusion in patients with chronic liver disease and thrombocytopenia [published online May 17, 2018]. Gastroenterology. doi: 10.1053/j.gastro.2018.05.025.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D69.59	Other secondary thrombocytopenia
D69.3	Immune thrombocytopenic purpura
D69.6	Thrombocytopenia, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC