Prior Authorization
Thrombocytopenia – Doptelet® (avatrombopag tablets for oral use)

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Cigna National Preferred Formulary Coverage Policy

Effective Date ........................................ 1/1/2021
Next Review Date ................................. 1/1/2022
Coverage Policy Number ...................... NPF622

FDA Indication(s)
1. Chronic Immune Thrombocytopenia. Approve if the individual meets the following criteria (A or B):
   A) Initial Therapy. Approve for 3 months if the individual meets all of the following (i, ii, iii, and iv):
      i. The individual must meet one of the following (a or b):
         a) The individual has a platelet count < 30 x 10⁹/L (< 30,000/µL); OR

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b) The individual has a platelet count < 50 x 10^9/L (< 50,000/μL) and according to the prescriber the individual is an increased risk of bleeding; AND

ii. The individual is ≥ 18 years of age; AND

iii. The agent is prescribed by or in consultation with a hematologist; AND

iv. The individual meets one of the following criteria (a or b):
   a) The individual has tried at least one other therapy.
      Note: Examples of therapies are systemic corticosteroids, intravenous immunoglobulin, anti-D immunoglobulin, Promacta® (eltrombopag tablets and oral suspension), Nplate® (romiplostim injection for subcutaneous use), Tavalisse™ (fostamatinib tablets), and rituximab; OR
   b) The individual has undergone splenectomy; OR

B) Continuation of Therapy. Approve for 1 year if the individual meets both of the following criteria: (i and ii):
   i. According to the prescriber the individual demonstrates a beneficial clinical response (e.g., increased platelet counts); AND
   ii. The individual remains at risk for bleeding complications.

2. Thrombocytopenia in Individuals with Chronic Liver Disease. Approve for 5 days if the individual meets the following criteria (A, B and C):
   A) The individual is an adult ≥ 18 years of age; AND
   B) The individual has a current platelet count < 50 x 10^9/L (< 50,000/µL); AND
   C) The individual is scheduled to undergo a procedure within 10 to 13 days after starting Doptelet therapy.

Conditions Not Covered

Avatrombopag (Doptelet®) is considered experimental, investigational or unproven for ANY other use.

Background

Overview
Doptelet, a thrombopoietin receptor agonist (TPO-RA), is indicated for the treatment of thrombocytopenia in adults with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. Also, Doptelet is indicated for the treatment of thrombocytopenia in adults with chronic liver disease who are scheduled to undergo a procedure. For chronic ITP initiate at 20 mg once daily (QD) and adjust the dose to maintain a platelet count ≥ 50 x 10^9/L. Do not exceed a dose of 40 mg QD. For chronic liver disease in patients undergoing a procedure, begin Doptelet dosing 10 to 13 days before the scheduled procedure. The recommended daily dose of Doptelet is based on the patient’s platelet count prior to the scheduled procedure. The dose is 60 mg (three tablets) QD for 5 days in patients with a platelet count < 40 x 10^9/L and 40 mg (two tablets) QD for 5 days for patients with a platelet count of 40 x 10^9/L to < 50 x 10^9/L. Doptelet should be given with food. Patients should undergo their procedure 5 to 8 days after the last Doptelet dose. For chronic ITP, Doptelet should be discontinued if the platelet count does not increase to ≥ 50 x 10^9/L within 4 weeks at the maximum dose of 40 mg QD. The safety and efficacy of Doptelet have not been established in pediatric patients.

Clinical Efficacy
The efficacy of Doptelet in adults with chronic ITP was assessed in a Phase III, double-blind, placebo-controlled trial in patients who had previously received one or more therapies and had an average baseline platelet count < 30 x 10^9/L. The median exposure duration was 26 weeks for Doptelet and 6 weeks for patients given placebo. Doptelet-treated patients had a longer duration of platelet counts ≥ 50 x 10^9/L in the absence of rescue therapy compared with patients who received placebo (12.4 vs 0 weeks, respectively; P < 0.001). Also, more patients receiving Doptelet had platelet counts ≥ 50 x 10^9/L (≥ 50,000/µL) at Day 8 compared with patients who received placebo (66% vs. 0.0%, respectively; P < 0.0001). The efficacy of Doptelet for the treatment of thrombocytopenia in patients with chronic liver disease who were scheduled to undergo a procedure was established in two identically-designed, multicenter, randomized, double-
blind, placebo-controlled trials (ADAPT-1 [n = 231] and ADAPT-2 [n = 204]).\textsuperscript{1,3} Patients were assigned to the low baseline platelet count cohort (< 40 x 10^9/L) or the high baseline platelet count cohort (≥ 40 to < 50 x 10^9/L) based on their baseline platelet count. In the trials the FDA-approved dosing was utilized for patients randomized (2:1) to receive Doptelet or placebo. Patients were scheduled to undergo their procedure (low, moderate, or high-bleeding risk) 5 to 8 days after their last treatment dose. In ADAPT-1, patients in the low- and high-baseline platelet count groups had baseline platelet counts of 31 x 10^9/L and 44 x 10^9/L, respectively. In ADAPT-2, patients in the low- and high-baseline platelet count groups had baseline platelet counts of 32 x 10^9/L and 44 x 10^9/L, respectively. The major efficacy outcome was the proportion of patients who did not require a platelet transfusion or any rescue procedure for bleeding after randomization and up to 7 days following an elective procedure. In ADAPT-1, this endpoint was statistically superior for patients given Doptelet compared with placebo (66% for Doptelet 60 mg vs. 23% with placebo and 88% for Doptelet 40 mg vs. 38% with placebo). Also, in ADAPT-2, the endpoint was statistically superior for patients given Doptelet compared with placebo (69% for Doptelet 60 mg vs. 35% with placebo and 88% for Doptelet vs. 33% with placebo).

Guidelines

In 2019 the American Society of Hematology updated guidelines for immune thrombocytopenia.\textsuperscript{4} There are several recommendations. For adults with ITP for at least 3 months who are corticosteroid-dependent or unresponsive to corticosteroid, a thrombopoietin receptor agonist (either Promacta\textsuperscript{®} [eltrombopag tablets and oral suspension] or Nplate\textsuperscript{®} [romiplostim injection for subcutaneous use]) or a splenectomy are recommended. In children with newly diagnosed ITP who have non-life-threatening mucosal bleeding, corticosteroids are recommended. For children who have non-life-threatening mucosal bleeding and do not respond to first-line treatment, thrombopoietin receptor agonists are recommended. Other treatment options in children and adults include intravenous immunoglobulin (IVIG), anti-D immunoglobulin, and rituximab.

References


Last Revision Details

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<th>Early annual revision</th>
<th>The following criteria changes were made:</th>
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<tr>
<td></td>
<td>1. <strong>Chronic Immune Thrombocytopenia:</strong> Criteria were divided into Initial Therapy and Continuation of Therapy. For Initial Therapy, the approval duration is for 3 months. Criteria were added that the patient has a platelet count &lt; 30 x 10^9/L (&lt; 30,000/µL) or that the patient had a platelet count &lt; 50 x 10^9/L (&lt; 50,000/µL) and according to the prescriber the patient is at an increased risk of bleeding. Also, regarding the requirement of a trial of at least one therapy, the word “systemic” was added before the word corticosteroids. Continuation of therapy is approved for 1 year in duration if, according to the prescriber, the patient demonstrates a beneficial clinical response (e.g., increase in platelet counts); AND the patient remains at risk for bleeding complications.</td>
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