rusfertide (Mimrylo™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO349

Split Fill Management*

Description

Rusfertide (Mimrylo) is a hepcidin mimetic administered as a subcutaneous injection.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
rusfertide (Mimrylo)	Erythrocytosis in Polycythemia Vera (PV)	9.5 mg vial	4 vials/28 days
		19 mg vial	
		28 mg vial	
		41 mg vial	
		54 mg vial	

Initial Evaluation

I. **Rusfertide (Mimrylo)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
   B. A diagnosis of **polycythemia vera (PV)** when the following are met:
      1. The member has a history of three or more phlebotomies in the past 28 weeks; **OR**
         i. The member has a history of five or more phlebotomies within the last year; **OR**
            a. Provider attestation that the member is experiencing phlebotomy intolerance; **AND**
      2. The member is currently being treated with at least one cytoreductive agent, unless ineffective, contraindicated, or not tolerated [e.g., hydroxyurea (HU), peginterferon alfa-2a (Pegasys), ropeginterferon alfa-2b (Besremi), ruxolitinib (Jakafi)].

II. Rusfertide (Mimrylo) is considered investigational when used for all other conditions, including but not limited to:
   A. Hemochromatosis

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, 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 (e.g., improved or stable hematocrit ≤45%, platelet and WBC count within normal range, reduction of phlebotomy occurrences, resolution of pruritis and/or erythema symptoms)

Supporting Evidence

I. Polycythemia Vera (PV) is considered a rare, chronic myeloproliferative disorder that causes overproduction of red blood cells, and manifests with symptoms of pruritus and microcirculatory disturbances (e.g., thrombosis, hemorrhage). Polycythemia vera occurs across all ages and populations, with a median age of 60 years at diagnosis and presents more commonly in men. Untreated or uncontrolled disease can lead to cardiovascular events, disease transformation (either to myelofibrosis or acute leukemia), and death.
II. The NCCN myeloproliferative neoplasms guideline provides treatment recommendations for PV based on risk stratification. Stratification is based on age and history of thrombotic events: low risk are patients <60 years old without prior thrombosis and high-risk are patients ≥60 years old and/or history of prior thrombosis. Low-risk management begins with phlebotomy and low-dose aspirin and escalation to cytoreductive therapy is based on response and symptom control. High-risk management recommends cytoreductive therapy alongside phlebotomy and low-dose aspirin, with adjustments made based on response to these treatments. The role of aspirin is to help treat initial symptoms while phlebotomy is to control hematocrit levels to <45% to decrease risk of disease worsening and complications.
III. Available cytoreductive agents include hydroxyurea (HU), peginterferon alfa-2a (Pegasys), ropeginterferon alfa-2b (Besremi), or ruxolitinib tablets (Jakafi). The NCCN guidelines currently list HU or Besremi as preferred agents for initial, high-risk treatment while Pegasys and Jakafi are alternative options. Jakafi is elevated to a category 1 recommendation as subsequent therapy for those who are high-risk and are intolerant or resistant to HU. Cytoreductive therapy for low-risk PV is reserved for those not adequately controlled with aspirin and phlebotomy. Guidelines prefer clinical trial or ropeginterferon alfa-2b (Besremi) before HU or Pegasys. Jakafi may be considered if subsequent options are needed.
IV. The NCCN guidelines include rusfertide (Mimrylo) as an additional agent to control and maintain hematocrit levels <45%, when there is frequent phlebotomy needs or phlebotomy intolerant. The guidelines do not define frequent phlebotomy, but the VERIFY trial included those that had at least three or more in the past 28 weeks or five or more in the past year. Low-risk use can be done alone or with cytoreductive therapy, while high-risk use is primarily as add-on treatment to existing cytoreductive therapy. It is a category 1 recommendation for both risk levels but does not replace cytoreductive therapy when it is otherwise indicated.

V. Rusfertide (Mimrylo) was FDA-approved for the treatment of erythrocytosis in adults with polycythemia vera (PV) based on a Phase 3, randomized, double-blind, placebo-controlled trial (VERIFY) that compared rusfertide (Mimrylo) with standard-of-care vs placebo with standard-of-care. Patients were randomized 1:1 and the primary endpoint was the proportion of patients who had a response between weeks 20 through 32. Response was defined as those who completed weeks 0 through 32 of the study, were not phlebotomy-eligible during weeks 20 through 32 and did not receive a phlebotomy during weeks 20 through 32.

VI. Baseline characteristics align with the typical epidemiology of this disease. This includes a median age of 57 years, primarily male, and a median phlebotomy occurrence of four in the last 28 weeks. About 45 to 48% of patients were considered high-risk and slightly more than half of individuals were on cytoreductive therapy (HU – 39%, interferons – 13%, JAK inhibitors – 3%).

VII. The primary endpoint was achieved with a response rate of 76.9% in the rusfertide (Mimrylo) group compared to placebo at 32.9% in week 32. In addition, secondary endpoints of mean number of phlebotomies (0.5, 1.8) and proportion of patients with all HCT values <45% (62.6%, 14.4%) throughout weeks 0 to 32 were found to be statistically significant and in favor of rusfertide (Mimrylo) over placebo, respectively. Patient-reported outcomes related to fatigue (PROMIS Fatigue) and overall myelofibrosis symptoms (MFSAF) at week 32 exhibited improvements from baseline, despite that the difference from placebo was not statistically significant. Subsequent data from the ongoing trial allowed those to switch to rusfertide (Mimrylo) from placebo from weeks 32 through 52 while the rusfertide (Mimrylo) group continued on treatment. The switch group noted an improved response rate of 77.9% at week 52 while the rusfertide (Mimrylo) group maintained the response at 84.1%.

VIII. In the first 32 weeks of the trial (part 1a), treatment-emergent adverse events (TEAE) included injection site reactions (55.9% vs 32.9%), anemia (15.9% vs 4.1%), and fatigue (15.9% vs 4.1%) in the rusfertide (Mimrylo) vs placebo group, respectively. While serious adverse events (AE) were reported higher in the placebo group (4.8%) than the rusfertide (Mimrylo) group (3.4%) with one thromboembolic event occurring in the rusfertide (Mimrylo) group. Discontinuation rates from TEAEs were higher in the rusfertide (Mimrylo) group than in the placebo group (5.5% vs 2.7%, respectively). Safety data for weeks 32 through 52 (part 1b) were comparable to part 1a, where those who switched from placebo to rusfertide experienced TEAEs of injection site reactions (32.9%), anemia (10%), and fatigue (9.3%). Serious side effects occurred in 2.6% of patients, and an additional thromboembolic event was reported. The discontinuation in this OLE portion was 2.6% of patients.

IX. The quality of evidence is considered moderate as the objective secondary endpoints help support the composite primary endpoint. In addition, the patient reported outcomes support clinical improvement in quality of life and ongoing trial data from the Phase 3 trial and Phase 2 trials (REVIVE and THRIVE) support the ongoing durability and safety of the medication.

X. Although the discontinuation rate is low, dosing instructions require a minimum of two weeks on the current dosage before making any dose modifications. These modifications are based on serial hematocrit testing to ensure appropriate disease and dose monitoring. Split fill ensures reduction of drug waste streamlined dose titration.

Investigational or Not Medically Necessary Uses

I. Rusfertide (Mimrylo) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Hemochromatosis

Appendix

Table 1: Rusfertide (Mimrylo) Weekly Dosing Instructions

Mimrylo Weekly Dose[†]	Dosing Instructions	Frequency During Each Week
9.5 mg	Single Injection	Once Weekly
19 mg		
28 mg		
41 mg		
54 mg		
69 mg	28 mg AND 41 mg	Once weekly on the Same Day
82 mg	41 mg AND 41 mg	
95 mg	Day 1: 54 mg Day 4 or 5: 41 mg	Day 1 and Day 4 or 5
108 mg	Day 1: 54 mg Day 4 or 5: 54 mg	

† Doses higher than 54 mg are administered as 2 injections. If the weekly dosage is greater than 82 mg, administer the first injection on day 1 and the second injection on day 4 or 5.

** The Moda Split Fill program is a physician-centric, patient engagement program intended to provide enhanced patient and physician support while accomplishing the goals of minimizing waste and avoiding incremental healthcare costs due to medication intolerance and unexpected change or termination of therapy regimen. Under the Split Fill program, the identified medications are programmed for fills of up to a 14 or 15-day supply for the duration of the first three months (86 or 90 days) of therapy. This program affords additional interactions with a specialty pharmacist, allowing more frequent assessments of side effects and barriers to adherence. Each fill is administered at half of the member cost-share, thereby reducing the economic burden if they must discontinue therapy mid-month.*

References

1. Mimrylo. Post-approval product dossier. Takeda Pharmaceuticals; August 2026.
2. Mimrylo. Prescribing Information. Takeda Pharmaceuticals; August 2026.
3. National Comprehensive Cancer Network. Myeloproliferative Neoplasms (Version 3.2026). https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed August 31, 2026.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
ruxolitinib (Jakafi®, Opzelura™) Policy	Intermediate or high-risk myelofibrosis
	Polycythemia vera

	Graft-Versus-Host Disease
	Atopic dermatitis
ropeginterferon alfa-2b-njft (Besremi®) Policy	Polycythemia vera
Peginterferon alfa-2a (Pegasys®) Policy	Polycythemia vera
	Essential thrombocythemia
	Chronic hepatitis B
	Chronic hepatitis D

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	11/2026