BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

BESREMI® (ropeginterferon alfa-2b-njft) for subcutaneous injection Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for BESREMI (ropeginterferon alfa-2b-njft)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Oncologist or Hematologist or is in consultation with an Oncologist or Hematologist

Indication
- Polycythemia vera

ORIGINAL EFFECTIVE DATE: 02/17/22 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/19/2026

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Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Has either all three major, or the first two major criteria plus the minor criterion of the World Health Organization diagnostic criteria (see Definitions section)
- Complete blood count with differential
- Blood smear
- Testing for Janus kinase 2 (JAK2) V617F in blood or Janus kinase 2 (JAK2) exon 12 mutation
- Serum erythropoietin
- Eye exam in those with diabetes or hypertension
- Serum triglycerides
- Liver enzymes and hepatic function tests
- Serum creatinine
- Negative pregnancy test in females with reproductive potential

Alternative Therapies
- Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for hydroxyurea

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- There is **NONE** of the following:
  - Severe psychiatric disorders, including severe depression, suicidal ideation, or suicide attempt
  - Hypersensitivity to interferons
  - Moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment
  - Active serious or untreated autoimmune disease
  - Immunosuppressed transplant recipient
  - Significant renal impairment with estimated glomerular filtration rate less than 30 mL/minute
  - Severe or unstable cardiovascular disease including uncontrolled hypertension, congestive heart failure greater than or equal to New York Heart Association Class 2, serious cardiac arrhythmia, significant coronary artery stenosis, unstable angina, or recent stroke or myocardial infarction

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (complete blood count, blood smear, JAK2 mutation testing, serum erythropoietin, eye exam, serum triglycerides, liver enzymes, hepatic function tests, serum creatinine, pregnancy test)
  - Supporting clinical documentation

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Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification

- Continues to be seen by an Oncologist or Hematologist or is in consultation with an Oncologist or Hematologist

Clinical Response

- Positive clinical response defined as **TWO** of the following:
  - Hematocrit less than 45 percent
  - Reduction in phlebotomy
  - Platelets less than or equal to 400 x 10^9/L
  - Reduction in spleen size
  - Absence of thromboembolic events

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- There is **NONE** of the following:
  - Severe psychiatric disorders, including severe depression, suicidal ideation, or suicide attempt
  - Hypersensitivity to interferons
  - Moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment
  - Active serious or untreated autoimmune disease
  - Immunosuppressed transplant recipient
  - Significant renal impairment with estimated glomerular filtration rate less than 30 mL/minute
  - Severe or unstable cardiovascular disease, including uncontrolled hypertension, congestive heart failure greater than or equal to New York Heart Association Class 2, serious cardiac arrhythmia, significant coronary artery stenosis, unstable angina, or recent stroke or myocardial infarction
- If clinically appropriate, withhold, reduce dose, or permanently discontinue based on severity, recurrence, persistence, or duration of the following adverse reactions:
  - Life threatening neuropsychiatric reactions
  - Endocrine disorders unmanageable during treatment
  - Cardiovascular toxicity
  - Severe anemia, leukopenia, thrombocytopenia
  - Severe allergic reactions
  - Pancreatitis

- Colitis
- Pulmonary toxicity
- Eye disorders
- Hepatic decompensation
- Severe renal impairment
- Severe or unstable cardiovascular disease

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in polycythemia vera
- Lab values confirming safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Polycythemia vera (PV) is a chronic myeloproliferative disorder that causes the bone marrow to produce too many red blood cells. The median age at presentation is 60 years. Patients often present with either arterial or venous vascular occlusive events. The events are predominantly coronary and cerebral but can involve the skin and gastrointestinal tract. Over time PV may evolve to MF, acute myeloid leukemia (AML), or myelodysplastic syndrome (MDS). The mainstay of therapy for PV is phlebotomy which removes excess red blood cells and lowers blood viscosity. In general, the goal of phlebotomy is to keep the hematocrit below 45% in men and 42% in women. When patients remain symptomatic despite phlebotomy, other options include hydroxyurea (with or without phlebotomy), interferon alfa, ruxolitinib, thalidomide, lenalidomide, anagrelide (in certain circumstances) and rarely, chlorambucil, melphalan, or busulfan. It is estimated that 25% of PV patients remain uncontrolled despite the use of existing standard therapies.

Besremi (ropeginterferon-alfa-2b-njft) is indicated for the treatment of adults with PV. Ropeinteferon-alfa-2b-njft uses a site-specific monopegylation technology that extends half-life to 7 days. It can be dosed every 2 weeks and extended to every 4 weeks after hematologic stability is achieved for at least 1 year. Ropeginterferon-alfa-2b-njft exhibit cellular effects in PV in the bone marrow by binding to transmembrane receptor termed interferon alfa receptor (IFNAR). Binding to IFNAR initiates a downstream signaling cascade through the activation of kinases, in particular Janus kinase 1 (JAK1) and tyrosine kinase 2 (TYK2) and activator of transcription (STAT) proteins. The actions involved in the therapeutic effects of interferon alfa in PV are not fully elucidated.

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

WHO diagnostic criteria polycythemia vera Diagnosis of PV requires meeting either all 3 major criteria, or the first 2 major criteria and the minor criterion¶
Major criteria:
1. Hemoglobin >16.5 g/dL in men
Hemoglobin >16.o g/dL in women
OR
Hematocrit >49% in men
Hematocrit >48% in women
OR
Increased red cell mass*
2. Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis) including prominent erythroid, granulocytic, and megakaryocytic proliferation with pleomorphic, mature megakaryocytes (differences in size)
3. Presence of *JAK2* V617F or *JAK2* exon 12 mutation
Minor criteria:
1. Subnormal serum erythropoietin level

* More than 25% above mean normal predicted value.
¶ Bone marrow biopsy **may not be required** in cases with sustained absolute erythrocytosis: hemoglobin levels >18.5 g/dL in men (hematocrit, 55.5%) or >16.5 g/dL in women (hematocrit, 49.5%) if major criterion 3 and the minor criterion are present. However, initial myelofibrosis (present in up to 20% of patients) can only be detected by performing a bone marrow biopsy; this finding may predict a more rapid progression to overt myelofibrosis (post-PV MF).
MF: myelofibrosis; PV: polycythemia vera; WHO: World Health Organization

Polycythemia vera:

Low-risk patients
Age ≤ 60 years and no history of thrombosis
High-risk patients:
Age > 60 years
History of thrombosis

Potential indications for cytoreductive therapy:
New thrombosis or disease related major bleeding
Frequent and/or persistent need for phlebotomy, but with poor tolerance for phlebotomy
Splenomegaly
Thrombocytosis

Leukocytosis
Disease related symptoms (e.g., pruritus, night sweats, fatigue)

Resources:

Besremi (ropeginterferon alfa-2b) product information, revised by PharmaEssentia USA Corporation. 11/2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 10, 2025.

Tefferi A. Clinical manifestations and diagnosis of polycythemia vera. In: UpToDate, Larsen RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated November 27, 2024. Accessed January 02, 2026.

Tefferi A. Polycythemia vera and secondary polycythemia: Treatment and prognosis. In: UpToDate, Larsen RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated February 27, 2024. Accessed January 02, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Myeloproliferative Neoplasms Version 2.2025 –Updated July 08, 2025. Available at https://www.nccn.org. Accessed January 02, 2026.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.