Clinical Policy: Ropeginterferon Alfa-2b-njft (BESREMi)

Reference Number: PA.CP.PHAR.570
Effective Date: 01/2022
Last Review Date: 01/2026

Description
Ropeginterferon alfa-2b-njft (BESREMi®) is an interferon alfa-2b.

FDA Approved Indication(s)
BESREMi® is indicated for the treatment of adults with polycythemia vera.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that BESREMi ® is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Polycythemia Vera (must meet all)**:**

1. Diagnosis of polycythemia vera;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. One of the following (a, b or c):
   a. One of the following (i or ii):
      i. Failure of hydroxyurea, unless clinically significant adverse effects are experienced or all are contraindicated;

      **Prior authorization may be required for hydroxyurea*

      ii. Request is for Stage IV or metastatic cancer;
   b. Member has symptomatic low risk-PV despite aspirin and phlebotomy therapy AND meets one of the following indications for cytoreductive therapy (i, ii, iii, iv, or v):
      i. New thrombosis or disease-related major bleeding;
      ii. Frequent phlebotomy or intolerant of phlebotomy;
      iii. Splenomegaly;
      iv. Progressive thrombocytosis and/or leukocytosis;
      v. Disease-related symptoms (e.g., pruritis, night sweats, fatigue);
   c. For use as substitute for peginterferon alfa-2a due to product unavailability (e.g., drug shortages);
5. Documentation of JAK2 V617F or JAK2 exon 12 mutation;
6. Member meets one of the following (a or b):
   a. For males: Documentation of hemoglobin level > 16.5 g/dL or hematocrit level of ≥ 49% or increased red cell mass;
   b. For females: Documentation hemoglobin level > 16 g/dL or a hematocrit level of≥ 48% or increased red cell mass;
7. Request meets one of the following (a or b):

a. Dose does not exceed 500 mcg every 2 weeks;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. NCCN Recommended Uses (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a-h):
   a. Systemic mastocytosis;
   b. Myelofibrosis;
   c. Essential thrombocythemia;
   d. Chronic myeloid leukemia (CML);
   e. T-cell leukemia/lymphoma;
   f. Mycosis fungoides/ Sézary syndrome;
   g. Primary cutaneous CD30+ T-cell lymphoproliferative disorders;
   h. Other NCCN recommendations listed as category 1, 2A, or 2B;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. One of the following (a, b or c):
   a. For use as substitute for peginterferon alfa-2a due to product unavailability (e.g., drug shortages);
   b. For CML as initial treatment during pregnancy;
   c. For essential thrombocythemia cytoreductive treatment with inadequate response or loss of response to prior cytoreductive therapy;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

C. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose change, request meets one of the following (a or b):
   a. For PV, one of the following (i or ii):
   i. For members with achievement of hematological stability for at least one year while on a stable dose of BESREMi, dose does not exceed 500 mcg every 4 weeks unless medical justification supports otherwise;
   ii. For members who have not yet achieved hematological stability, dose does not exceed 500 mcg every 2 weeks;

b. New dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CML: chronic myeloid leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
PV: polycythemia vera

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hydroxyurea (Droxia®, Hydrea®)	15 to 20 mg/kg/day	20 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Existence of, or history of severe psychiatric disorders, particularly severe depression, suicidal ideation or suicide attempt
  - Hypersensitivity to interferon, including interferon alfa-2b, or to any component of BESREMi
  - Moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment
  - History or presence of active serious or untreated autoimmune disease
  - Immunosuppressed transplant recipients
- Boxed warning(s):
  - Risk of Serious Disorders: Interferon alfa products may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders.

Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders.

Appendix D: General Information

- Per NCCN,
  - Low-risk PV: age < 60 years and no prior history of thrombosis
  - High-risk PV: age ≥ 60 years and/or prior history of thrombosis
- Per NCCN, for high risk PCV patients, preferred regimens for cytoreductive therapy include hydroxyurea or ropeginterferon alfa-2b-njft.
- Per NCCN, for low-risk PV patients, ropeginterferon alfa-2b-njft is the only preferred regimen for cytoreductive therapy. Other recommended regimens include hydroxyurea or peginterferon alfa-2a.
- Per Prescribing Information, hematological parameters are stabilized when hematocrit < 45%, platelets < 400 x 10^9/L, and leukocytes less than 10 x 10^9/L.
- Symptoms of disease progression include fatigue, early satiety, abdominal discomfort, inactivity, problems with concentration, night sweats, pruritus, bone pain (diffuse not joint pain or arthritis), fever (> 100 F), unintentional weight loss last 6 months.
- Poor tolerance to phlebotomy is defined as recurrent episodes of post-phlebotomy syncope despite appropriate preventive interventions.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Polycythemia vera	Starting dose: 100 mcg SC injection every 2 weeks (50 mcg if receiving hydroxyurea). Increase the dose by 50 mcg every 2 weeks until hematological parameters are stabilized (hematocrit < 45%, platelets < 400 x 10^9/L, and leukocytes less than 10 x 10^9/L). Maintain the two week dosing interval at which hematological stability is achieved for at least 1 year. After achievement of hematological stability for at least 1 year on a stable dose, the dosing interval may be expanded to every 4 weeks.	500 mcg every 2 weeks

VI. Product Availability

Injection: 500 mcg/mL solution in a single-dose prefilled syringe

VII. References

1. BESREMi Prescribing Information. Burlington, MA. PharmaEssentia Corporation; April 2024. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761166s000lbl.pdf. Accessed November 6, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 25, 2025.

3. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed November 25, 2025.
4. National Comprehensive Cancer Network. Systemic Mastocytosis Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed: November 25, 2025.
5. ClinicalTrials.gov. Safety Study of Pegylated Interferon Alpha 2b to treat polycythemia vera (PEGINVERA). Available at https://clinicaltrials.gov/ct2/show/NCT01193699. Accessed November 6, 2025.
6. Barbui T, Thiele J, Gisslinger H, et al. The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion. Blood Cancer J. 2018 Feb; 8(2): 15.
7. McMullin MF, Harrison CN, Ali Set al; BSH Committee. A guideline for the diagnosis and management of polycythemia vera. A British Society for Hematology Guideline. British Journal Hematology. 2019 Jan; 184(2):176-191.
8. Gisslinger H, Zagrijtschuk O, Buxhofer-Ausch V, et al. Ropeginterferon alfa-2b, a novel IFNα-2b, induces high response rates with low toxicity in patients with polycythemia vera. Blood. 2015 Oct 8; 126(15): 1762–1769.
9. Tefferi A and Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023;98:1465-1487.
10. Marchetti M, Vannucchi AM, Griesshammer, et al. Appropriate management of polycythaemia vera with cytoreductive drug therapy: European LeukemiaNet 2021 recommendations. Lancet Haematol. 2022 April;9(4):e301-e311. doi: 10.1016/S2352-3026(22)00046-1.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologics
J9999	Not otherwise classified, antineoplastic drugs

Reviews, Revisions, and Approvals	Date
Policy created.	01/2022
1Q 2023 annual review: Revised initial criteria from "JAK2V617K" to "JAK2V617F" to reflect correct mutation studied in population; corrected the polycythemia vera hemoglobin and hematocrit criteria to read ">" the minimum values for men and women hemoglobin and hematocrit per the WHO diagnostic criteria; for continued therapy, added criteria that for members with achievement of hematological stability for at least one year while on a stable dose of BESREMi, dose does not exceed 500 mcg every 4 weeks unless medical justification supports otherwise; added definition of	01/2023

Reviews, Revisions, and Approvals	Date
hematological stability in Appendix D per PI; references reviewed and updated.	
1Q 2024 annual review: no significant changes; for Appendix D, added Besremi as preferred regimen for cytoreductive therapy for high risk PCV; added HCPCS codes [C9399, J9999]; references reviewed and updated.	01/2024
Removed peginterferon alfa-2a as therapeutic alternative as no longer a preferred cytoreductive therapy for high-risk PV per NCCN; Added option for usage in low-risk PV with indications for cytoreductive therapy per NCCN; for Appendix D, added definition for low-risk and high-risk PV, removed peginterferon alfa-2a from preferred regimen for cytoreductive therapy for high-risk PV, added examples of symptoms of disease progression per NCCN.	04/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025
1Q 2026 annual review: extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition; for PV, added option for usage as for use as substitute for peginterferon alfa-2a due to product unavailability per NCCN; added off-label criterion for systemic mastocytosis, myelofibrosis, essential thrombocythemia, CML, T-cell leukemia/lymphoma, Mycosis fungoides/ Sézary syndrome, Primary cutaneous CD30+ T-cell lymphoproliferative disorders per NCCN; references reviewed and updated.	01/2026