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

Reference Number: PA.CP.PHAR.570
Effective Date: 01/2022
Last Review Date: 04/2024

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 or b):
   a. Failure of hydroxyurea, unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for hydroxyurea*
   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);
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: 6 months

B. 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. Polycythemia Vera (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.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose change, request meets one of the following (a, b or c):
   a. 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;
   b. For members who have not yet achieved hematological stability, dose does not exceed 500 mcg every 2 weeks;
   c. New 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. 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.LTSS.PHAR.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

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 for all relevant lines of business 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 <	500 mcg every 2 weeks

Indication	Dosing Regimen	Maximum Dose
	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.	

VI. Product Availability

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

VII. References

1. BESREMi Prescribing Information. Burlington, MA. PharmaEssentia Corporation; November 2021. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761166s000lbl.pdf. Accessed February 13, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 13, 2024.
3. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 1.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed February 13, 2024.
4. ClinicalTrials.gov. Safety Study of Pegylated Interferon Alpha 2b to treat polycythemia vera (PEGINVERA). Available at https://clinicaltrials.gov/ct2/show/NCT01193699. Accessed February 13, 2024.
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6. 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.
7. 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.
8. Tefferi A and Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023;98:1465-1487.
9. 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.

Reviews, Revisions, and Approvals	Date
Policy created.	01/2022

Reviews, Revisions, and Approvals	Date
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 hematological stability in Appendix D per PI; references reviewed and updated.	01/2023
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