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

Reference Number: LA.PHAR.570
Effective Date: 09.29.23
Last Review Date: 02.13.26~~02.06.25~~ Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

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

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

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 Louisiana Healthcare Connections® that BESREMi ® is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of PV;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. ~~4.~~ One of the following (a ~~or~~ b, or c):

a. ~~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);

c. For use as substitute for peginterferon alfa-2a due to product unavailability (e.g., drug shortages);

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~~5.~~4. Documentation of JAK2 V617F mutation;
~~6.~~5. 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.~~6. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: ~~6~~ 12 months

B. ~~Other diagnoses/indications~~ (must meet ~~1 or 2~~all)**:**
1. ~~If this~~ Diagnosis of one of the following (a, b, c, or d):
   a. Systemic mastocytosis;
   b. Myelofibrosis;
   c. Essential thrombocythemia;
   d. Chronic myeloid leukemia (CML);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. For use as substitute for peginterferon alfa-2a due to product unavailability (e.g., drug ~~has recently (~~shortages);
   b. For CML as initial treatment during pregnancy;
5. Dose is within ~~the last 6 months) undergone a label change (e.g., newly~~ FDA maximum limit for any FDA-approved indication~~, age expansion, new dosing~~ or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

** Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
~~1.~~ If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to ~~) that is not yet reflected in this policy, refer to LA~~LA.PMN.25~~5~~5
   a.
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy ~~for the relevant line of business:~~ LA.PMN.53.

II. Continued Therapy

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A. ~~**Polycythemia Vera**~~**All Indications in Section I** (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving BESREMi for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a~~, b~~ or ~~c~~b):*
   a. For PV, one of the following (i or ii):
      ~~a.~~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;
      ~~b.~~ii. For members who have not yet achieved hematological stability, dose does not exceed 500 mcg every 2 weeks;
   ~~c.~~b. ~~New dose~~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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

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

~~If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to~~

~~1. **Other diagnoses/indications** LA.PMN.255~~

B. (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy ~~for the relevant line of business:~~ LA.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~~ies~~ LA.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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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.

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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 PV 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

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1. BESREMi Prescribing Information. Burlington, MA. PharmaEssentia Corporation; ~~November 2021.~~April 2024. Available at: https://www.besremi.com/. Accessed ~~February 13, 2024.~~: November 6, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed ~~February 13, 2024~~November 25, 2025.
3. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version ~~1.2024~~2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed ~~February 13, 2024~~: November 25, 2025.
~~3.~~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.
~~4.~~5. 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~~: November 6, 2025.
~~5.~~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.
~~6.~~7. McMullin MF, Harrison CN, Ali S, et 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.~~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.

~~8.~~9. Tefferi A and Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023;98:1465-1487.
~~9.~~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.

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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	LDH Approval Date
Policy created.	05.01.23	08.28.23
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.	04.05.24	07.10.24
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.	02.06.25	05.19.25
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, and CML per NCCN; references reviewed and updated.	02.13.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

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