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

Reference Number: CP.PHAR.570
Effective Date: 03.01.22
Last Review Date: 02.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

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 health plans affiliated with Centene Corporation® 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. Failure of hydroxyurea or peginterferon alfa-2a, unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for hydroxyurea and peginterferon alfa-2a*
5. Documentation of JAK2 V617F mutation;
6. Member meets one of the following:
   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*).

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

Approval duration: 6 months

B. 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 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 for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene 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):*
   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*).

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

Approval duration: 12 months

B. 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 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 for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

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
Pegasys®, Pegasys ProClick® (peginterferon alfa-2a)	Varies	Varies

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, for high risk PCV patients, preferred regimens for cytoreductive therapy 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.

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; November 2021. Available at https://www.besremi.com/. Accessed November 2, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 2, 2022.
3. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 3.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed November 2, 2022.
4. ClinicalTrials.gov. Safety Study of Pegylated Interferon Alpha 2b to Treat Polycythemia Vera (PEGINVERA). Available at https://clinicaltrials.gov/ct2/show/NCT01193699. Accessed November 2, 2022.
5. 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. McMullin MF, Harrison CN, Ali S, Cargo C, Chen F, Ewing J, Garg M, Godfrey A, S SK, McLornan DP, Nangalia J, Sekhar M, Wadelin F, Mead AJ; 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	11.30.21	02.22
Revised initial criteria from "JAK2V617K" to "JAK2V617F" to reflect correct mutation studied in population.	10.19.22	
1Q 2023 annual review: 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.	11.02.22	02.23

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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.