09-J4000-19

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Reviewed: 12/14/22

Revised: 01/15/23

Subject: Ropeginterferon alfa-2b-njft (Besremi)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Polycythemia vera is a type of myeloproliferative neoplasm caused by the overproduction of blood cells in the bone marrow. An abnormally high number of red blood cells causes the blood to thicken and not flow normally through small blood vessels. Patients may experience headaches, fatigue, enlarged spleen, dry skin, and are at risk of blood clots. A genetic mutation in the JAK2 gene has been identified in approximately 90% of cases. Ropeginterferon alfa-2b-njft (Besremi) is FDA-approved for the treatment of adults with polycythemia vera. Interferon alfa binds to a receptor which initiates a signal cascade to activate kinases (JAK1 and TYK2) and a transcription (STAT) protein. The mechanism to generate a clinical benefit in polycythemia vera is not completely understood.

Ropeginterferon alfa-2b-njft was evaluated in a single-arm trial in 51 adults with polycythemia vera over 7.5 years. There were approximately 84% treatment experienced patients and 16% newly diagnosed. There were 33% of patients receiving hydroxyurea when they were enrolled in the study. The patients were tapered off of hydroxyurea over the first 12 weeks to avoid toxicity. The complete hematological response (CHR) was defined as hematocrit less than 45% and no phlebotomy in the preceding 2 months, platelets less than or equal to 400 x 10^9/L and leukocytes less than or equal to 10 x 10^9/L, normal spleen size, and absence of thromboembolic events. The CHR was 61% (31/51) (95% CI: 46, 74) during the treatment period with a median time to response of 7.8 months. The median duration of response was 14.3 months (95% CI: 5.5, 30.1). Approximately 80% of patients achieved a hematological response based on hematocrit, platelets, and leukocytes. There were at least 53% of patients who completed 60 months of treatment and at least 28 patients were able to increase their dosing interval from every 2 weeks to every 4 weeks at a median time of 21.5 months. The most common adverse reactions reported in greater than 40% of patients were influenza-like illness, arthralgia, fatigue, pruritus, nasopharyngitis, and musculoskeletal pain.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore,

coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of ropeginterferon alfa-2b-njft (Besremi) **meets the definition of medical necessity** for the following when **ALL** of the indication- specific criteria are met:

1. Polycythemia vera (PV)
    a. The member does not have any of the following:
        i. Severe psychiatric disorder (e.g., severe depression, suicidal ideation or suicide attempt)
        ii. Hepatic impairment (Child Pugh Class B or C)
        iii. History of or presence of an active serious or untreated autoimmune disease
        iv. History of transplant and receiving immunosuppression
        v. The member does not have severe renal impairment (eGFR less than 30 ml/min/1.73 m^2)
    b. The initial dose does not exceed 100 mcg by subcutaneous injection every 2 weeks[a] and titrated up to a maximum of 500 mcg every 2 weeks
2. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    a. **ONE** of the following is met:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    b. The dose does not exceed the maximum FDA-approved dose maximum and frequency

Approval duration: 6 months

Continuation of ropeginterferon alfa-2b-njft (Besremi) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for ropeginterferon alfa-2b-njft has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of polycythemia vera or another FDA-approved or NCCN supported diagnosis, **OR** the member has previously met **ALL** indication-specific criteria.
2. The member has a beneficial response to treatment - (For PV, a beneficial response includes hematocrit less than 45%, platelets less than or equal to 400 x 10^9/L, leukocytes less than or equal to 10 x 10^9/L)– documentation must be submitted
3. The dose does not exceed 500 mcg every 2 weeks[b]

Approval duration: 12 months

[a]Note: If the member is transitioning from hydroxyurea the initial dose should not exceed 50 mcg by subcutaneous injection every two weeks (while hydroxyurea dose is tapered) up to a maximum of 500 mcg until hematological parameters are stabilized

[b]Note: If the member's hematologic parameters have been stable for at least 1 year, a trial of extending the dosing interval to every 4 weeks should be considered

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Treatment of adults with polycythemia vera: 100 mcg by subcutaneous injection every 2 weeks (50 mcg if receiving hydroxyurea)
- Increase the dose by 50 mcg every 2 weeks (up to a maximum of 500 mcg) until hematological parameters are stabilized (hematocrit less than 45%, platelets less than 400 x 10^9/L, and leukocytes less than 10 x 10^9/L
- Maintain the two week dosing interval for at least 1 year and may increase dosing interval to every 4 weeks if hematological stability is achieved for at least one year
- Interrupt or discontinue dosing if certain adverse reactions occur
- Monitor closely during the titration phase and perform complete blood counts regularly.
- Phlebotomy as rescue treatment to normalize blood hyperviscosity may be necessary during the titration phase.

Dose Adjustments

- Avoid use in patients with eGFR < 30 mL/min
- Use is contraindicated in patients with hepatic impairment (Child-Pugh class B or C)

Drug Availability

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

PRECAUTIONS:

Boxed Warning

- Risk of serious disorders: Interferon 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.

Contraindications

- Existence of, or history of severe psychiatric disorders, particularly severe depression, suicidal ideation or suicide attempt.

- Hypersensitivity to interferon or to any component of ropeginterferon alfa-2b-njft
- Hepatic impairment (Child-Pugh B or C)
- History or presence of active serious or untreated autoimmune disease
- Immunosuppressed transplant recipients

Precautions/Warnings

- Closely monitor, dose reduce or discontinue therapy for any of the following:
    - Depression and suicide
    - Endocrine toxicity
    - Cardiovascular toxicity
    - Decreased peripheral blood counts
    - Hypersensitivity reactions
    - Pancreatitis
    - Colitis
    - Pulmonary toxicity (pulmonary infiltrates or pulmonary function impairment)
    - Ophthalmologic toxicity
    - Hyperlipidemia (monitor triglycerides)
    - Hepatotoxicity
    - Renal toxicity
    - Dental and periodontal toxicity
    - Dermatologic toxicity
    - Driving and operating machinery if dizziness, somnolence or hallucination occurs

BILLING/CODING INFORMATION:

HCPCS Coding

J3590	Unclassified biologicals

ICD-10 Diagnosis Codes That Support Medical Necessity

D45	Polycythemia vera

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None.

RELATED GUIDELINES:

None.

OTHER:

None.

REFERENCES:

1. Besremi Prescribing Information. PharmaEssentia USA Corporation. Burlington, MA. November 2021
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc. Accessed 12/01/22.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Accessed 12/01/22.
4. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 12/01/22.
5. National Organization of Rare Diseases. https://rarediseases.org/rare-diseases
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2022 [cited 12/01/22]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/14/22.

GUIDELINE UPDATE INFORMATION:

04/01/22	New Medical Coverage Guideline.
01/15/23	Review and revision to guideline; including removing step through a prior therapy and update to references.