Besremi (ropeginterferon alfa-2b-njft)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Besremi is indicated for the treatment of adults with polycythemia vera.

POLICY

Required Documentation
The following information is necessary to initiate the prior authorization review:

A. Initial requests: Sumbission of medical records documenting diagnosis of polycythemia vera.
B. Continuation requests: Submission of chat notes or medical records documenting a benefit from therapy (e.g., reduction or stabilization in red blood cell volume, reduction or stabilization in spleen size, improvement of thromobocytosis and/or leukocytosis).

Prescriber Specialties
The medication must be prescribed by or in consultation with a hepatologist or oncologist.

Criteria for Initial Approval
Polycythemia Vera

Authorization of 12 months may be granted for treatment of polycythemia vera when all of the following criteria are met:

A. The member has a diagnosis of polycythemia vera (PV).
B. The member is 18 years of age or older.
C. The medication is prescribed by or in consultation with a hepatologist or oncologist.

Continuation of Therapy

Authorization of 12 months may be granted for all members (including new members) requesting continuation of therapy when the member is experiencing a positive response to therapy (e.g., reduction or stabilization in red blood cell volume, reduction or stabilization in spleen size, improvement of thromobocytosis and/or leukocytosis).

Besremi (ropeginterferon alfa-2b-njft) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limit

Besremi 500 mcg/ml prefilled syringe – 2 prefilled syringes per 28 days

CLINICAL RATIONALE

Besremi is an interferon alfa-2b subcutaneous injection indicated for the treatment of adults with polycuthmia vera. Polycythemia vera, along with essential thrombocytopenia and myelofibrosis, belongs to a group of chronic heterogenous hematologic malignancies known as breakpoint cluster-Abelson (BCR-ABL1)-negative myeloproliferative neoplasms. Polycythemia vera is primarily characterized by elevated blood cell counts, thrombotic and hemorrhagic predisposition, a variety of symptoms, and cumulative risk of progression to myelofibrosis and/or leukemic evolution over time. Polycythemia vera is often initially suspected due to abnormal blood work, but the most common clinical manifestations of polycythemia vera include palpable splenomegaly, aquagenic pruritus, fatigue, erythromelalgia (i.e., rare condition that causes episodes or burning pain and redness usually in the feet), and microcirculatory disturbances. Splenomegaly affects approximately 30% to 40% of polycythemia patients and is usually associated with advanced disease. Thrombosis is the greatest contributor to morbidity and mortality in patients with polycythemia vera. In addition, about 5% to 6% of patients with polycythemia vera progress to post-polycythemia vera myelofibrosis, and 2% to 14% of patients progress to acute myeloid leukemia at 10 years. Due to these complications, life expectancy is reduced in patients with polycythemia vera.

The NCCN Guidelines® recommend hydroxyurea as initial therapy in high-risk patients (i.e., ≥ 60 years of age and/or prior history of thrombosis), and peginterferon alfa-2a (Pegasys) could be considered in younger patients and in pregnant patients requiring cytoreductive therapy. Oral ruxolitinib (Jakafi) is recommended in high-risk patients who have an inadequate response to hydroxyurea or peginterferon alfa-2a. These guidelines were written prior to the FDA approval of Besremi. The guidelines note that ropeginterferon alfa-2b-njft (Besremi) is an emerging treatment for low-risk polycythemia vera and has been approved by the European Medicines Agency as a first-line treatment of for adult polycythemia vera without symptomatic splenomegaly.

The clinical efficacy section for Besremi in patients with polycythemia vera is composed of a phase I/II, single-arm, dose-escalation trial (PEGINVERA); a phase III, randomized controlled trial vs. hydroxyurea (PROUD-PV) and its extension trial (CONTINUATION-PV). When evalutating the clinical trials, the FDA noted that PROUD-PV and CONTINUATION-PV had several statistical issues with the design and analysis. However, the PEGINVERA study and the change in hematology laboratory parameters in PROUD-PV as mechanistic and confirmatory evidence established the efficacy of Besremi (ropeginterferon alfa-2b-njft) in the treatment of polycythemia vera without symptomatic splenomegaly. Overall, Besremi (ropeginterferon alfa-2b-njft) improved complete hematological response in 61% of patients with polycythemia (61% with splenomegaly) with a median duration of response of about 14 months in PEGINVERA. However, in PROUD-PV, in patients with polycythemia vera (~10% with splenomegaly), Besremi (ropeginterferon alfa-2b-njft) did not demonstrate non-inferiority to hydroxyurea at 12 months for complete hematological response with normal spleen size or complete hematologic response but response to Besremi (ropeginterferon alfa-2b-njft) improved over time up to 36 months.

Besremi carries a boxed warning for risk of life-threatening neuropsychatric, autoimmue, ischemic, and infectious disorders. Besremi is contraindicated in patients with existence of or history of severe psychiatric disorders, particularly severe depression, suicidal ideation, or suicide attempt; moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment; history or presence of active serious or untreated autoimmune disease; and immunosuppressed transplant recipients. Adverse events that occurred in > 40% of patients include influenza-like illness, arthralgia, fatigue, pruritis, nasopharyngitis, and musculoskeletal pain.

For patients not receiving hydroxyurea therapy, the recommended starting dose for Besremi is 100 mcg subcutaneously every 2 weeks. For patients transitioning from hydroxyurea therapy, the recommended starting dose for Besremi is 50 mcg subcutaneously every 2 weeks in combination with hydroxyurea. The dose of Besremi in all patients should be increased by 50 mcg every 2 weeks (up to a maximum of 500 mcg) until the hematological parameters are stabilized (i.e., hematocrit < 45%, platelets < 400 x 109/L, and leukocytes < 10 x 109/L). For patients receiving hydroxyurea therapy, hydroxyurea should be gradually tapered off by reducing the total biweekly dose by 20% to 40% every 2 weeks during weeks 3 through 12 and should be discontinued by week 13. The 2-week dosing interval of Besremi at which hematological stability is achieved should be maintained for at least 1 year; thereafter, the dosing interval may be increased to every 4 weeks.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

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POLICY HISTORY

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