BESREMi®
(ropeginterferon alfa-2b-njft)
INJECTION

Ropeginterferon alfa-2b-njft (BESREMi) is a recommended option by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for both low- and high-risk PV in multiple treatment settings[1]

Recommended option by the NCCN Guidelines®

NCCN, National Comprehensive Cancer Network; PV, polycythemia vera.

INDICATION

BESREMi is indicated for the treatment of adults with polycythemia vera

IMPORTANT SAFETY INFORMATION

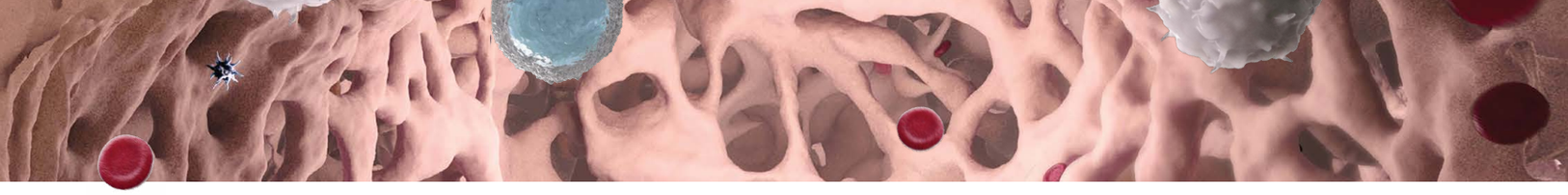
WARNING: RISK OF SERIOUS DISORDERS

Interferon alfa products may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping therapy.

CONTRAINDICATIONS

- Existence of, or history of severe psychiatric disorders, particularly severe depression, suicidal ideation, or suicide attempt
- Hypersensitivity to interferons including interferon alfa-2b or any of the inactive ingredients 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

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.



NCCN Guidelines® Recommendations for ropeginterferon alfa-2b-njft (BESREMi)

Included as an option in multiple treatment settings for patients with low-risk PV[1]

Patients with low-risk PV*

NCCN Guideline initial treatment option recommendations

- **Manage cardiovascular risk factors**
- **Aspirin**
- **Phlebotomy (to maintain hematocrit <45%)**
- **Ropeginterferon alfa-2b-njft (category 2B†)**

*Cytoreductive therapy is not recommended as initial treatment.
†Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

BESREMi is recommended as **first-line therapy** for **low-risk** patients, supporting the need to treat early in the course of PV.[1]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

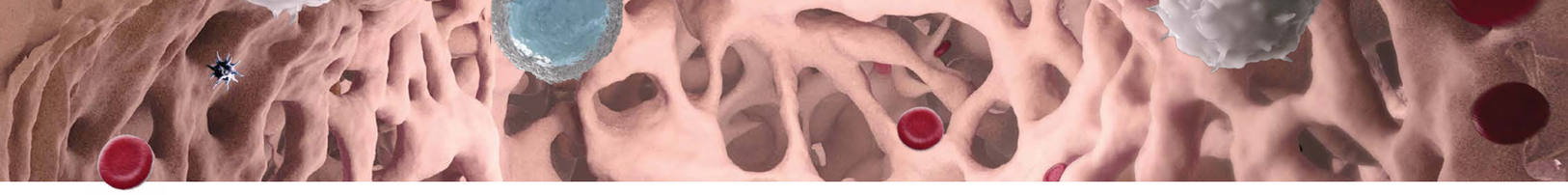
- Depression and Suicide: Life-threatening or fatal neuropsychiatric reactions have occurred in patients receiving interferon alfa-2b products, including BESREMi. These reactions may occur in patients with and without previous psychiatric illness.

  Other central nervous system effects, including suicidal ideation, attempted suicide, aggression, bipolar disorder, mania and confusion have been observed with other interferon alfa products.

  Closely monitor patients for any symptoms of psychiatric disorders and consider psychiatric consultation and treatment if such symptoms emerge. If psychiatric symptoms worsen, it is recommended to discontinue BESREMi therapy.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.

BESREMi® (ropeginterferon alfa-2b-njft) INJECTION



NCCN Guidelines® Recommendations for ropeginterferon alfa-2b-njft (BESREMi)

Included as an option in multiple treatment settings for patients with high-risk PV[1]

Patients with high-risk PV

NCCN Guideline treatment recommendations include

Ropeginterferon alfa-2b-njft as an initial treatment option (category 2A[‡])

or

Ropeginterferon alfa-2b-njft as an option after inadequate response or loss of response with prior cytoreductive therapy[§] (category 2A[‡])

[‡]Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

[§]Potential indications for change of cytoreductive therapy include Intolerance or resistance to hydroxyurea or peginterferon alfa-2a; new thrombosis or disease-related major bleeding; frequent phlebotomy or intolerant of phlebotomy; splenomegaly; progressive thrombocytosis and/or leukocytosis; disease-related symptoms (eg, pruritus, night sweats, fatigue).

See NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms, V.2.2022, for complete recommendations. NCCN makes no representations or warranties of any kind regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

BESREMi is recommended for both low-risk and high-risk patients with PV in multiple treatment settings.[1]

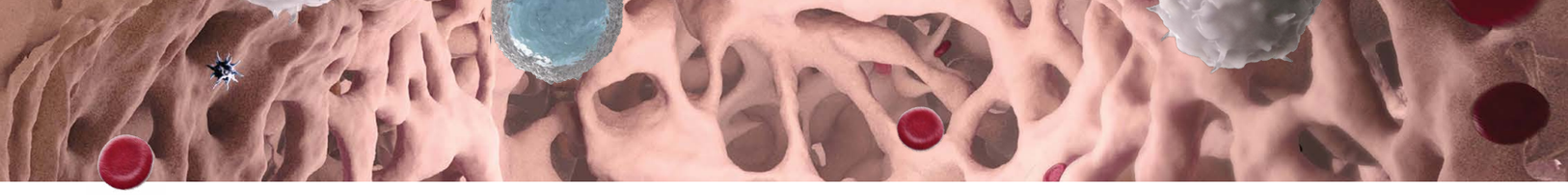
IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- Endocrine Toxicity: These toxicities may include worsening hypothyroidism and hyperthyroidism. Do not use BESREMi in patients with active serious or untreated endocrine disorders associated with autoimmune disease. Evaluate thyroid function in patients who develop symptoms suggestive of thyroid disease during BESREMi therapy. Discontinue BESREMi in patients who develop endocrine disorders that cannot be adequately managed during treatment with BESREMi.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.

BESREMi® (ropeginterferon alfa-2b-njft) INJECTION



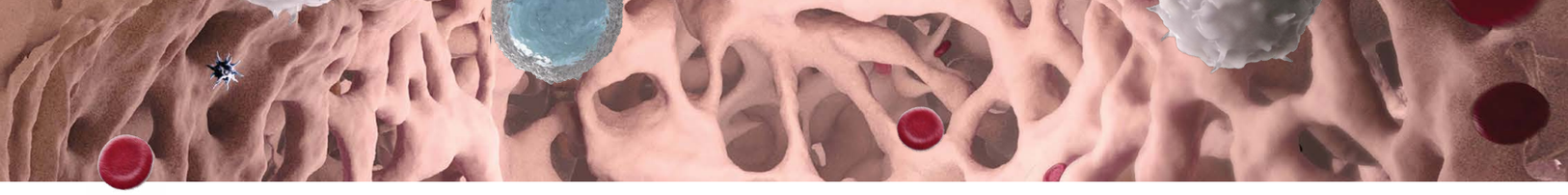
IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- Cardiovascular Toxicity: Toxicities may include cardiomyopathy, myocardial infarction, atrial fibrillation and coronary artery ischemia. Patients with a history of cardiovascular disorders should be closely monitored for cardiovascular toxicity during BESREMi therapy. Avoid use of BESREMi in patients with severe or unstable cardiovascular disease, (e.g., uncontrolled hypertension, congestive heart failure (≥ NYHA class 2), serious cardiac arrhythmia, significant coronary artery stenosis, unstable angina) or recent stroke or myocardial infarction.
- Decreased Peripheral Blood Counts: These toxicities may include thrombocytopenia (increasing the risk of bleeding), anemia, and leukopenia (increasing the risk of infection). Monitor complete blood counts at baseline, during titration and every 3-6 months during the maintenance phase. Monitor patients for signs and symptoms of infection or bleeding.
- Hypersensitivity Reactions: Toxicities may include serious, acute hypersensitivity reactions (e.g., urticaria, angioedema, bronchoconstriction, anaphylaxis). If such reactions occur, discontinue BESREMi and institute appropriate medical therapy immediately. Transient rashes may not necessitate interruption of treatment.
- Pancreatitis: Pancreatitis has occurred in 2.2% of patients receiving BESREMi. Symptoms may include nausea, vomiting, upper abdominal pain, bloating, and fever. Patients may experience elevated lipase, amylase, white blood cell count, or altered renal/hepatic function. Interrupt BESREMi treatment in patients with possible pancreatitis and evaluate promptly. Consider discontinuation of BESREMi in patients with confirmed pancreatitis.
- Colitis: Fatal and serious ulcerative or hemorrhagic/ischemic colitis have occurred in patients receiving interferon alfa products, some cases starting as early as 12 weeks after start of treatment. Symptoms may include abdominal pain, bloody diarrhea, and fever. Discontinue BESREMi in patients who develop these signs or symptoms. Colitis may resolve within 1 to 3 weeks of stopping treatment.
- Pulmonary Toxicity: Pulmonary toxicity may manifest as dyspnea, pulmonary infiltrates, pneumonia, bronchiolitis obliterans, interstitial pneumonitis, pulmonary hypertension, and sarcoidosis. Some events have resulted in respiratory failure or death. Discontinue BESREMi in patients who develop pulmonary infiltrates or pulmonary function impairment.
- Ophthalmologic Toxicity: These toxicities may include severe eye disorders such as retinopathy, retinal hemorrhage, retinal exudates, retinal detachment and retinal artery or vein occlusion which may result in blindness. During BESREMi therapy, 23% of patients were identified with an eye disorder. Eyes disorders ≥5% included cataract (6%) and dry eye (5%). Advise patients to have eye examinations before and during BESREMi therapy, specifically in those patients with a retinopathy-associated disease such as diabetes mellitus or hypertension. Evaluate eye symptoms promptly. Discontinue BESREMi in patients who develop new or worsening eye disorders.
- Hyperlipidemia: Elevated triglycerides may result in pancreatitis. Monitor serum triglycerides before BESREMi treatment and intermittently during therapy and manage when elevated. Consider discontinuation of BESREMi in patients with persistently, markedly elevated triglycerides.
- Hepatotoxicity: These toxicities may include increases in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) and bilirubin. Liver enzyme elevations have also been reported in patients after long-term BESREMi therapy. Monitor liver enzymes and hepatic function at baseline and during BESREMi treatment. Discontinue BESREMi in patients who develop evidence of hepatic decompensation (characterized by jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome or variceal hemorrhage) during treatment
- Renal Toxicity: Monitor serum creatinine at baseline and during therapy. Avoid use of BESREMi in patients with eGFR <30 mL/min. Discontinue BESREMi if severe renal impairment develops during treatment.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.

BESREMi®
(ropeginterferon alfa-2b-njft)
INJECTION



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- Dental and Periodontal Toxicity: These toxicities may include dental and periodontal disorders, which may lead to loss of teeth. In addition, dry mouth could have a damaging effect on teeth and mucous membranes of the mouth during long-term treatment with BESREMi. Patients should have good oral hygiene and regular dental examinations.
- Dermatologic Toxicity: These toxicities have included skin rash, pruritus, alopecia, erythema, psoriasis, xeroderma, dermatitis acneiform, hyperkeratosis, and hyperhidrosis. Consider discontinuation of BESREMi if clinically significant dermatologic toxicity occurs.
- Driving and Operating Machinery: BESREMi may impact the ability to drive and use machinery. Patients should not drive or use heavy machinery until they know how BESREMi affects their abilities. Patients who experience dizziness, somnolence or hallucination during BESREMi therapy should avoid driving or using machinery.
- Embryo-Fetal Toxicity: Based on the mechanism of action, BESREMi can cause fetal harm when administered to a pregnant woman. Pregnancy testing is recommended in females of reproductive potential prior to treatment with BESREMi. Advise females of reproductive potential to use an effective method of contraception during treatment with BESREMi and for at least 8 weeks after the final dose.

ADVERSE REACTIONS

The most common adverse reactions reported in > 40% of patients in the PEGINVERA study (n=51) were influenza-like illness, arthralgia, fatigue, pruritis, nasopharyngitis, and musculoskeletal pain. In the pooled safety population (n=178), the most common adverse reactions greater than 10%, were liver enzyme elevations (20%), leukopenia (20%), thrombocytopenia (19%), arthralgia (13%), fatigue (12%), myalgia (11%), and influenza-like illness (11%).

DRUG INTERACTIONS

Patients on BESREMi who are receiving concomitant drugs which are CYP450 substrates with a narrow therapeutic index should be monitored to inform the need for dosage modification for these concomitant drugs. Avoid use with myelosuppressive agents and monitor patients receiving the combination for effects of excessive myelosuppression. Avoid use with narcotics, hypnotics or sedatives and monitor patients receiving the combination for effects of excessive CNS toxicity.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on mechanism of action and the role of interferon alfa in pregnancy and fetal development, BESREMi may cause fetal harm and should be assumed to have abortifacient potential when administered to a pregnant woman. There are adverse effects on maternal and fetal outcomes associated with polycythemia vera in pregnancy. Advise pregnant women of the potential risk to a fetus.
- Lactation: There are no data on the presence of BESREMi in human or animal milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed children from BESREMi, advise women not to breastfeed during treatment and for 8 weeks after the final dose.
- Females of Reproductive Potential: BESREMi may cause embryo-fetal harm when administered to a pregnant woman. Pregnancy testing prior to BESREMi treatment is recommended for females of reproductive potential. Advise female patients of reproductive potential to use effective contraception during treatment with BESREMi and for at least 8 weeks after the final dose.
- Pediatric Use: Safety and effectiveness in pediatric patients have not been established.
- Geriatric Use: In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other therapy.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.

BESREMi®
(ropeginterferon alfa-2b-njft)
INJECTION

BESREMi®
(ropeginterferon alfa-2b-njft)
INJECTION

Discover more at BESREMiHCP.com

BESREMi targets the bone marrow, the source of PV, so you can address the underlying disease[2]

- **High and durable rates of complete hematologic response over 7.5 years, across a broad range of patients with PV[2]**

- **A manageable long-term safety profile[2]**

- **An innovative monopegylated interferon with PK properties that allow dosing once every 2 weeks[2]**
  - After hematologic stability is achieved for at least 1 year, the dosing interval may be expanded to 1 dose every 4 weeks

PK, pharmacokinetic.

INDICATION

BESREMi is indicated for the treatment of adults with polycythemia vera

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS DISORDERS

Interferon alfa products may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping therapy.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed May 18, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** Besremi. Package insert. PharmaEssentia Corporation; 2021.

PharmaEssentia™