

**NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY UPDATED TO RECOMMEND BESREMI® (ROPEGINTERFERON ALFA-2B-NJFT) AS A PREFERRED INTERVENTION FOR POLYCYTHEMIA VERA**

*BESREMI moved to preferred intervention based on superior efficacy, safety and evidence for both high-risk and low-risk patients, regardless of treatment history*

**May 23, 2023, Burlington, MA** – [PharmaEssentia USA Corporation](#), a subsidiary of PharmaEssentia Corporation (TPEX:6446, LuxSE: PHECA, PHECR), a global biopharmaceutical innovator based in Taiwan leveraging deep expertise and proven scientific principles to deliver new biologics in hematology and oncology, today announced that the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®) have been updated to include BESREMI® (ropeginterferon alfa-2b-njft) as a preferred therapeutic option for the treatment of adults with both high and low-risk polycythemia vera (PV), regardless of treatment history.

“Importantly, the NCCN Guidelines update includes moving BESREMI to preferred status, reinforcing to treating physicians and patients that with its broad utility, BESREMI is recommended for proactively treating PV,” said John Mascarenhas, M.D., professor of medicine, hematology, and medical oncology at the Icahn School of Medicine at Mount Sinai in New York.

The NCCN is a well-recognized, not-for-profit alliance of leading cancer centers in the United States. Its treatment practice guidelines, which are reviewed and updated on a continual basis to reflect the most current evidence, are widely respected and followed by the U.S. physician community and serve to inform and facilitate coverage decisions with payers for oncology therapies. Based on its growing body of supporting clinical evidence and broad label, BESREMI is now categorized by the latest NCCN update, released on May 19, 2023, as a preferred intervention based on superior efficacy, safety and evidence<sup>1</sup>, as well as a category 2A therapy, which means that there is uniform NCCN consensus that the intervention is appropriate<sup>1</sup>.

“This recent update to treatment guidelines by NCCN represents the community’s recognition of the value of BESREMI as a therapeutic option for all adults with PV, regardless of their treatment history,” said Raymond Urbanski, M.D., Ph.D., U.S. Head of Clinical Development and Medical Affairs. “Given its deep, durable control over the disease beyond the symptoms, we’re continuing to study BESREMI in PV, as well as other myeloproliferative neoplasms (MPNs) and hematologic malignancies.”

**About BESREMI® (ropeginterferon alfa-2b-njft)**

BESREMI is an innovative monopegylated, long-acting interferon. With its unique pegylation technology, BESREMI has a long duration of activity in the body and is aimed to be administered once every two weeks (or every four weeks with hematological stability for at least one year), allowing flexible dosing that helps meet the individual needs of patients.

BESREMI has orphan drug designation for the treatment of polycythemia vera (PV) in adults in the United States. The product was approved by the European Medicines Agency (EMA) in 2019, in Taiwan in 2020, in South Korea and the United States in 2021, and has recently received approval in Japan. The drug candidate was invented by PharmaEssentia and is

manufactured in the company's Taichung plant, which was cGMP certified by TFDA in 2017 and by EMA in January 2018. PharmaEssentia retains full global intellectual property rights for the product in all indications.

### **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

### **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.

- **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.

- **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 ( $\geq$  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  $\geq$ 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.
- **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 accompanying full [Prescribing Information](#), including **Boxed Warning**.

## About Polycythemia Vera (PV)

Polycythemia vera (PV) is a cancer originating from a disease-initiating stem cell in the bone marrow resulting in a chronic increase of red blood cells, white blood cells and platelets. PV may result in cardiovascular complications such as thrombosis and embolism, and often transforms to secondary myelofibrosis or leukemia. While the molecular mechanism underlying PV is still subject of intense research, current results point to a set of acquired mutations, the most important being a mutant form of JAK2.<sup>4</sup>

## About PharmaEssentia

PharmaEssentia (TPEX: 6446, LuxSE: PHECA, PHECR), headquartered in Taipei, Taiwan, is a rapidly growing, fully integrated global biopharmaceutical innovator. Leveraging proven scientific principles and deep expertise in commercializing medicines, PharmaEssentia aims to build upon its discovery-based innovation to deliver biologics for challenging diseases in hematology, oncology and immunology. With an approved product and a diversifying pipeline, PharmaEssentia strives to be an essential partner in cancer care by reshaping the treatment path for diseases with significant unmet medical needs. Founded in 2003 by a team of Taiwanese-American executives and renowned scientists from U.S. biotechnology and pharmaceutical companies, today PharmaEssentia is expanding its global presence with operations in the U.S., Japan, China, and Korea, along with a world-class biologics production facility in Taichung, Taiwan, and a new research and development facility in the Boston, Massachusetts, area.

For more information about PharmaEssentia USA, visit the [website](#), [LinkedIn](#) or [Twitter](#).

### **Forward Looking Statement**

This press release may contain forward-looking statements, including statements regarding the commercialization plans and expectations for commercializing BESREMi in the United States, and the potential benefits or competitive position of BESREMi. For those statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 and similar legislation and regulations under Taiwanese law. These forward-looking statements are based on management expectations and assumptions as of the date of this press release, and actual results may differ materially from those in these forward-looking statements as a result of various factors. These factors include whether BESREMi is successfully commercialized and adopted by physicians and patients, the extent to which reimbursement is available for BESREMi, risks and uncertainties related to the initiation, timing, progress and results of our research and development programs, preclinical studies, clinical trials, and regulatory submissions. We do not undertake to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof.

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### **References:**

1. NCCN Guidelines, page 60.

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