



Positive Quality Intervention: Ropeginterferon alfa-2b-njft (BESREMi) Use in Polycythemia Vera

Description: The purpose of this PQI is to discuss the use of ropeginterferon alfa-2b-njft (BESREMi) in the management of polycythemia vera (PV).

Background: Ropeginterferon alfa-2b-njft is indicated for the treatment of adults with polycythemia vera. It was approved by the FDA in 2021 for PV regardless of treatment history and the first interferon therapy specifically approved for PV.¹ NCCN has designated ropeginterferon alfa-2b-njft as a preferred therapy option for high and low-risk PV, regardless of treatment history.² It is a subcutaneous injection given by a health care professional or by patient/caregiver, administered once every two weeks with the potential to change to every four weeks dosing after achievement of hematological stability for at least 1 year on a stable dose, offering patients a reduction in pill burden.¹ The CONTINUATION-PV study found that 71% of patients achieved complete hematologic response (CHR) on ropeginterferon alfa-2b-njft at 36 months, compared to 51% of patients achieving CHR on hydroxyurea.³ Ropeginterferon alfa-2b-njft also achieved CHR in 80% (based only on lab parameters) with all three counts (hematocrit, platelets, and WBCs) over the 7 year observation period in the majority of patients, according to the PEGINVERA study.⁴ Ropeginterferon alfa-2b-njft also showed similar rates of adverse reactions compared to hydroxyurea, with both arms sharing the incidence rate of thromboembolic adverse events of 1.2% per patient year.⁵

PQI Process:¹

- Confirm diagnosis for polycythemia vera
- Assess the patient's need for ropeginterferon alfa-2b-njft versus other cytoreductive options (i.e., hydroxyurea, peginterferon)
- Assess the patient's medical history for contraindications to ropeginterferon alfa-2b-njft
 - Hypersensitivity to interferons, including interferon alfa-2b, or any component of the formulation; existence of, or history of severe psychiatric disorders, particularly severe depression, suicidal ideation, or suicide attempt; moderate (Child-Pugh class B) or severe (Child-Pugh class C) hepatic impairment; history or presence of active serious or untreated autoimmune disease; immunosuppressed transplant recipients
 - Avoid in patients with uncontrolled hypertension, congestive heart failure, arrhythmias, significant arterial stenosis, unstable angina, recent stroke or myocardial infarction
- Assess pregnancy status in females of reproductive age
- Review the patient's medication history for use of hydroxyurea in anticipation of possible need for ropeginterferon alfa-2b-njft dosage adjustment as detailed below
- Monitoring
 - Perform blood counts at baseline, every 2 weeks during titration and at least every 3-6 months during maintenance treatment
 - Eye exams at baseline and during treatment
 - Monitor for signs of suicidal ideation
 - Monitor cardiovascular toxicity
 - Discontinue if any of the following occur: medically unmanageable endocrine toxicities, severe cardiac disease, hypersensitivity reactions, pancreatitis, colitis, pulmonary function impairment
- AE
 - Boxed warning: Risk of Serious Disorders: Interferon alfa products may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders
 - Most common AE³: Flu like symptoms, itching, sore throat, hypersensitivity reactions,

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ophthalmologic toxicity, hepatotoxicity, endocrine toxicity, depression and suicide

- Dose Modification

	Starting Dose	Increasing Dose	Maximum Dose
Transitioning from Hydroxyurea (HU)	50 mcg SQ every 2 weeks in combo with HU	50 mcg SQ every 2 weeks until hematological parameters stabilize (hematocrit <45%, platelets <400,000/mm ³ , and leukocytes <10,000/mm ³) Gradually taper the HU by reducing the total biweekly hydroxyurea dose by 20% to 40% every 2 weeks during weeks 3-12; discontinue hydroxyurea by week 13	500 mcg every 2 weeks
Not on Hydroxyurea	100 mcg every 2 weeks		

- Patients with impaired hepatic function: no adjustment; use is contraindicated in Child-Pugh class B/C
- Patients with impaired renal function: avoid use in patients with eGFR <30 mL/minute or if renal impairment occurs during treatment
- Patients who experience adverse reactions: dosage adjustments and discontinuation recommendations for LFT elevations, cytopenia, and depression are listed in the [package insert](#)

Patient-Centered Activities:¹

- Patient Education

- Advise patients to read the FDA-approved medication guide and instructions for use patient labeling
 - Ensure eye exams and labs are scheduled prior to initiating treatment and as clinically necessary
 - Educate on good oral hygiene and regular dental examination
- Counsel on proper storage, preparation, and administration techniques if administering at home
- Instruct patients to report any signs of an allergic reaction, like rash, hives, itching, red, swollen, blistered or peeling skin with or without fever, wheezing, tightness in the chest or throat, trouble breathing, or swelling of the mouth, face, lips, tongue, or throat
- Direct patients to report any signs of depression, suicidal thoughts, or abnormal thinking
- Inform patients to report symptoms of tiredness, frequent urination, and increase in thirst
- Advise females of reproductive age to use an effective method of contraception during treatment and for at least 8 weeks after the final dose, as ropeginterferon alfa-2b-njft may cause fetal harm
- Advise women not to breastfeed during treatment and for 8 weeks after the final dose

References:

1. [BESREMi \(ropeginterferon alfa-2b-njft\) package insert.](#)
2. Myeloproliferative Neoplasms. NCCN. Published May 19, 2023. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf.
3. Gisslinger H, Klade C, Georgiev P, Krochmalczyk D, Gercheva-Kyuchukova L, Egyed M, Rossiev V, Dulicek P, Illes A, Pylypenko H, Sivcheva L, Mayer J, Yablokova V, Krejcy K, Grohmann-Izay B, Hasselbalch HC, Kralovics R, Kiladjian JJ; PROUD-PV Study Group. Ropiginterferon alfa-2b versus standard therapy for polycythaemia vera (PROUD-PV and CONTINUATION-PV): a randomised, non-inferiority, phase 3 trial and its extension study. *Lancet Haematol.* 2020 Mar;7(3):e196-e208. doi: 10.1016/S2352-3026(19)30236-4. Epub 2020 Jan 31. Erratum in: *Lancet Haematol.* 2020 Feb 25;: PMID: 32014125.
4. Heinz Gisslinger, Veronika Buxhofer-Ausch, Josef Thaler, Ernst Forjan, Ella Willenbacher, Dominik Wolf, Robert Kralovics, Bettina Gisslinger, Margarete Stampfl-Mattersberger, Alexander Egle, Thomas Melchardt, Sonja Burgstaller, Martin Schalling, Maria-Theresa Krauth, Richard Greil, Pavla Kadlecova, Michael Zoerer, Victoria Empson, Barbara Grohmann-Izay, Christoph Klade; Long-Term Efficacy and Safety of Ropiginterferon Alfa-2b in Patients with Polycythemia Vera — Final Phase I/II Pegivera Study Results. *Blood* 2018; 132 (Supplement 1): 3030. doi: <https://doi.org/10.1182/blood-2018-99-118584>.
5. Heinz Gisslinger, Klade C, Georgiev P, et al. Polycythemia Vera Patients Respond Better to Ropiginterferon Alfa-2b Than HU/BAT Irrespective of Pretreatment or Mutational Status; Results from 5 Years' Treatment in a Randomized, Controlled Setting in the PROUD-PV/Continuation-PV Trials. 2021;138(Supplement 1):3660-3660. doi:<https://doi.org/10.1182/blood-2021-152328>.