Dear Dr. \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_,

Myeloproliferative blood disorders, in which the bone marrow makes too many blood cells, can increase blood viscosity and the risk of a stroke, heart attack, pulmonary embolism or venous thrombosis, while also causing enlargement of the spleen (splenomegaly) due to increasing blood cell production in that organ (extramedullary hematopoiesis). The basis for the denial for interferon is the belief that it is an “experimental” form of therapy for this disease when, in fact, it is a well-established form of therapy in polycythemia vera (PV). The purpose of this letter is to provide you with information on the medical necessity of this treatment, provide peer-reviewed literature to support this position, and ask that interferon be covered for PV patients.

Two of the characteristics of PV that are most difficult to treat are intractable pruritus and exuberant extramedullary hematopoiesis with intractable splenomegaly. Beyond frequent phlebotomies, chemotherapy is one of the few treatment options available to treat PV patients. However, chemotherapy can permanently damage already genetically unstable PV stem cells and is not always effective in controlling the extramedullary hematopoiesis and splenomegaly. There is also a significant risk of acute myeloid leukemia following exposure of PV patients to chemotherapy. Splenic irradiation or splenectomy has been used to treat intractable splenomegaly, but neither is totally effective nor without risk. Splenic irradiation is a temporary measure that often causes profound neutropenia leading to infectious complications, while splenectomy is associated with a variety of morbidities including intra-abdominal venous thrombosis and an increase in hepatic extramedullary hematopoiesis and marrow blood cell production requiring chemotherapy.

Interferon is one of the only forms of therapy that has been conclusively shown to effectively treat PV by controlling pruritus and alleviating splenomegaly. By way of background, there are 4 types of interferon: Human leukocyte interferon (Multiferon), a recombinant interferon (Intron A) manufactured by Schering/Merck, a pegylated interferon manufactured by Schering /Merck known as PEG-Intron and another PEG product manufactured by Roche known as Pegasys. In the past 20 years, there have been 17 published clinical trials of the use of interferon in PV. In all 17 studies there was either a complete elimination of the need for continued phlebotomy or a substantial reduction in phlebotomy rates. The studies also showed a rapid reduction of platelet and white cell counts, relief of pruritus and reduction in splenomegaly. Furthermore, with pegylated interferon, complete and durable hematologic and molecular remissions have been observed. We have attached a list of journal articles describing some of these studies.

Human leukocyte interferon is no longer used in the United States for a variety of reasons and we are not seeking coverage of this product for treatment of PV. There is currently no evidence of qualitative differences between recombinant interferon and the two forms of pegylated interferon (PEGIFN). Further studies may demonstrate the advantages of a particular form of interferon; however, at this time, such data do not exist. Therefore, recombinant interferon and the two forms of PEGIFN are equivalent therapies and should be considered medically necessary for the treatment of PV with phlebotomy requirements, intractable pruritus and/or exuberant extramedullary hematopoiesis with intractable splenomegaly. The number of clinical studies supporting its use clearly establish that it is not an “experimental” treatment. Finally, in this regard, we should also point out that recombinant interferons were widely used with success for years in a companion disorder, chronic myelogenous leukemia, until targeted therapy became available for that disorder.

We, therefore, ask you to reconsider your current coverage policy for interferon treatment for PV. Based on the scientific literature, interferon should be considered a medically necessary treatment option for patients with PV (ICD-9 code 238.4/ICD-10 code D45). The recommended dosing of pegylated interferon is to initiate treatment at 45 mcg/week escalating to 90 mcg/week or higher if the desired effects have not occurred by three months. Rarely, a patient may require as much as 180 mcg/week to achieve the desired effects of the drug. Some patients may have to remain on such treatment indefinitely, but in others the drug can be discontinued with durable remissions and will still be effective if a relapse should occur. The dose of Intron A, recombinant interferon alpha-2b, is initially 1,000,000 U three times a week and increasing to 3,000,000 U three times a week as tolerated.

Sincerely,

**References**

Kiladjian JJ, Cassinat B, Turlure P, et al. High molecular response rate of polycythemia vera patients treated with pegylated interferon alpha-2a. Blood 2006; 108(6): 2037-40.

Kiladjian JJ, Cassinat B, Chevret S, et al. Pegylated interferon-alfa-2a induces complete hematologic and molecular responses with low toxicity in polycythemia vera. Blood 2008; 112(8):3065-72.

Quintas-Cardama, A., et al., Pegylated Interferon Alfa-2a Yields High Rates of Hematologic and Molecular response in Patients With Advanced Essential Thrombocythemia and Polycythemia Vera. Journal of Clinical Oncology 2009; 27(32): 5418-24.

Gowin K, Thapaliya P, Samuelsson J, et al. [Experience with pegylated interferon alpha-2a in advanced myeloproliferative neoplasms in an international cohort of 118 patients.](http://www.ncbi.nlm.nih.gov/pubmed/22419578) Haematologica 2012; 97(10): 1570-3.