Disclaimer: The information provided here should NOT be used as a substitute for seeking professional medical diagnosis, treatment, or care. You should NOT rely on any information in these pages to replace consultations with qualified health professionals. The information presented in this document comes from Friedreich's Ataxia medical professionals trying to be helpful to FA families that might be facing an off-label use situation. Although this information has been reviewed by a number of physicians expert in FA, we do not offer this information as medical advice, but rather as thoughtful reflections you might want to consider, along with your own team of medical professionals.

PATIENT GUIDE: SPECIAL CONSIDERATIONS IN THE OFF-LABEL USE OF ERYTHROPOIETIN (EPO)

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One of the agents proposed for development as a potential treatment in FA is erythropoietin, an agent currently approved for other uses. In patients considering off-label use in FA, the choice of who might use it, how to ensure safety, and how to determine if it has an effect, should follow the same guidelines as in our more general **Guide for off-label Drug Use in Friedreich ataxia.** However**,** there are special considerations that any patient considering use of erythropoietin must understand.

Rationale for use of erythropoietin- Erythropoietin is a hormone that our body makes (in the kidneys) and releases into the blood, where it acts on bone marrow to control production of red blood cells. The drug that has been developed consists of synthetic erythropoietin, which is then made into a suitable form for injection. It is used for increasing red blood cell counts in people with a variety of forms of anemia (such as anemia in people with kidney disease and anemia following chemotherapy).

The proposed use of erythropoietin in FA derives from findings in laboratories examining cells from patients with FA. These cells are grown (cultured) in test tubes and then treated with erythropoietin. It has been found that the erythropoietin can increase levels of frataxin when administered to such cultured cells. This appears to occur in several types of cells, but nerve cells have never been tested. The effect is modest, with increases in frataxin levels of about 50%. Although small, this increase could conceivably give some degree of clinical benefit.

Based on these studies, erythropoietin has been given in an initial trial to 11 FA patients (5000 U three times per week). The study was short (8 weeks) and there was no placebo group. In 8 of 10 patients, frataxin levels in white blood cells increased (although in only 6 was it greater than 25%). Five of 11 patients had improved scores on a clinical rating scale. A second study followed these patients over the course of 6 months (at 2000 U three times per week). At the 6 month point, 5 of 8 still had increased frataxin levels. At six months, patients also improved mildly, though the improvement did not match the change in frataxin level and the improvement varied based on how it was measured (suggesting that it may not be reliable). Thus the data from these studies suggest that there may be a possibility that erythropoietin can be useful in FA.

Dosing of erythropoietin: There have been no studies to find out the best dose of erythropoietin in FA. The dose chosen for the reported studies was a single dose amount in each case. There have been no studies comparing different dose levels for optimum effectiveness/efficacy. Thus the ideal dose for producing benefit or for minimizing side effects is unclear. Furthermore, whether erythropoietin can actually get to the brain or nervous system at any of these doses is unknown.

To provide perspective, for anemia associated with renal failure (the most common clinical use of erythropoietin) the dose is typically 3000-10000 units per week. This leads to a restoration of hemoglobin levels to normal (a 33% increase in hemoglobin).

Risk associated with erythropoietin therapy: Erythropoietin therapy can be dangerous. The two most common serious side effects are an increase in blood pressure and an increase in red blood cell count beyond the normal range. The latter places individuals at higher risk of stroke or heart attack due to increases in blood thickness. In general, the unsafe level of hemoglobin is about 20% above normal levels, a level the doses of erythropoietin used in the FA trials would be expected to reach. This can be controlled by systematically removing a unit of blood. In the 6 month trial of erythropoietin in FA, 4 of eight patients required this procedure (called phlebotomy) to control red blood cell count.

However, because of the heart disease associated with FA in some patients, phlebotomy is a somewhat risky procedure. FA heart disease reflects not only the potential for cardiac ischemia (less blood flow) in FA and also the increased stiffness of the heart in FA. The cardiac implications are of particular concern in patients with more advanced FA. This increases the risk of using erythropoietin in patients with FA beyond that of most non-FA individuals.

Recent studies have also suggested that erythropoietin can increase the risk of cancer in people and that it can increase the damage associated with stroke. These studies are controversial and there is no reason that patients with FA should be more susceptible to these side effects.

Based on these risks, safety monitoring for erythropoietin use at the beginning should include at a minimum weekly blood counts, and blood pressure checks. In addition, should phlebotomy be necessary, it most likely requires admission to a care unit experienced in this procedure.

Monitoring of effects: If individuals choose to pursue off-label use of erythropoietin, its effect can be assessed by a physician using the same tests as for all other FA studies. However, if erythropoietin does raise frataxin levels in patients, how fast and how much benefit it provides in day-to-day abilities are unknown. It is possible that the benefit could occur only after weeks to months of therapy. In addition, it could simply slow disease progression and a person might worsen but at a slightly slower rate. This type of response is very hard to be certain about in a single individual. Thus, the early response of patients may be of modest benefit in determining whether erythropoietin is effective, particularly since the progression of FA varies widely between patients.