

Anemia, EPO, Kidney Failure—and You

If you're on dialysis, you most likely have *anemia*—a shortage of red blood cells. And, you probably take EPO to treat it. New studies have led to a warning by the Food and Drug Administration (FDA) about EPO. Don't panic! Read on, and we'll tell you what this warning means to *you*.

Why You Need Anemia Treatment

Red blood cells carry oxygen to your body's cells. Anemia starves your cells of oxygen. This causes symptoms like:

- Severe fatigue
- Muscle weakness
- Shortness of breath
- Feeling cold all the time
- Pale skin, lips, gums, and nails
- Dizziness
- Trouble focusing your mind

These symptoms are hard to deal with. People with anemia say things like, *“Even walking from the bedroom to the kitchen I rest after every two or three steps. I stop, because I don't have the strength to walk with. My quality of life has dropped so much that it's almost unbearable. I can't do anything to help my wife.”*¹ Some have even quit their jobs—too tired to work—then later found out anemia could be treated.

In the long run, anemia can damage your heart. When there is less oxygen in your blood, your heart speeds up. Beating faster all the time makes your heart work much harder. The muscle of

the main pumping chamber can become thick and overgrown, a problem called *left ventricular hypertrophy* (LVH). LVH can make your heart so stiff that it can't pump as well. This can lead to heart failure.² It is vital for you to have your anemia treated.

How Anemia is Treated

In kidney failure, the main cause of anemia is a loss of *erythropoietin* (EPO). Kidneys sense the amount of oxygen in your blood. When levels drop, they send out EPO, a hormone that tells your bone marrow to make red blood cells. As kidneys fail, they make less EPO, so you make fewer red blood cells.

The treatment for anemia due to kidney failure is EPO. Three drugs on the market are *erythrocyte* (red blood cell) *stimulating agents* (ESAs), or cloned forms of EPO:

- **Epogen**[®] (epoetin alfa, Amgen)
- **Aranesp**[®] (darbepoetin alfa, Amgen)
- **Procrit**[®] (epoetin alfa, Ortho Biotech)

Epogen and Procrit are the same drug. Epogen is used in dialysis, while Procrit is used in predialysis. Aranesp is a new form of EPO that lasts longer. It is used for people who are predialysis *or* on dialysis. All three drugs are used to treat other causes of anemia as well.

Iron is also needed to treat anemia; it is the building block the body uses to form new red blood cells. Iron works best when it is given through a vein.

Anemia Treatment Goals in Dialysis

Each month, you have a blood test for hemoglobin (Hb or Hgb). Hb picks up oxygen in your lungs and brings it to all of your cells. In healthy women, a normal Hb is 12.1 to 15.1 grams per deciliter (g/dL); in men, 13.8 to 17.2 g/dL. (“Normal” levels vary by lab.)

In people on dialysis, the Hb targets are below normal: 11 g/dL or greater in women *and* men. No one should be kept at a Hb of 13 g/dL or greater.³

Why are the target levels for anemia treatment less than normal? Because the Guidelines are based on research—and studies have not proven that a higher target is safe for those on dialysis.

FDA Black Box Warnings

The FDA issues a black box warning when research suggests that a drug may cause harm in some cases. A black box warning was placed on all ESAs in March, 2007, due to new research.

None of these new studies was of people on dialysis.

In people with cancer, four new studies found problems when EPO was used:

1. A number of studies have linked anemia with poor outcomes in

people with head and neck cancers.^{4,5,6,7} But in the Danish Head and Neck Cancer study, patients given EPO to reach a (normal) Hb target of 14 to 15.5 g/dL did worse than those who took a placebo.

2. A study of cancer patients who were not on chemo found that EPO did not reduce the need for transfusions (the target Hb was 12 g/dL). Patients who took EPO were also more likely to die.⁸
3. A study of whether EPO would improve quality of life in people with non-small cell lung cancer was stopped early. More people in the EPO group died than those who took a placebo. Target Hb was 12 to 14 g/dL.
4. Hoffman-La Roche was testing a new ESA in people with non-small cell lung cancer (Hb target of 11 to 13 g/dL). Those who took the drug were more likely to die. The study was stopped early.

The FDA also looked at two studies in chronic kidney disease (CKD) before dialysis:

1. The CHOIR study found that patients in a higher Hb group (target of 13.5 g/dL) had more adverse events like heart problems, hospital stays, or death than those in a lower Hb group (target of 11.3 g/dL).⁹

2. The CREATE study failed to show that full correction of anemia in CKD (target of 13 to 15 g/dL) would prevent heart damage. This study used epoetin beta, a drug that is not sold in the U.S.¹⁰

EPO and Quality of Life

Day-to-day quality of life may affect you more than a risk of a poor outcome. Research has shown much higher quality of life when dialysis anemia is treated with EPO.^{11,12,13,14}

In fact, a 48-72 week long Swedish study randomly assigned 416 patients (predialysis, on hemodialysis, or on peritoneal dialysis) to one of two Hb groups. One group had a target Hb of 13.5 to 16 g/dL (normal). The other group had a target Hb of 9 to 12 g/dL. This study found *no* higher risk of adverse events or death. The higher Hb group also had better quality of life.¹⁵

What You Should Do

Keep taking your EPO. The risk of anemia itself is far greater than any risk of taking the drug when it is used according to current guidelines. On the Black Box Warning, the FDA suggests using the lowest dose that will help you avoid blood transfusions. Your iron levels need to be kept in the target range so you have the building blocks you need to make red blood cells. This will allow your EPO to work.

Inflammation from an infection can also keep your body from using EPO. This is called EPO-resistance. Be sure to tell your care team about any fever, swelling, redness in your access, or other illness so it can be treated. This can help you need less EPO.

Getting more dialysis helps the red blood cells you *do* have to live longer. This means you may need less EPO to have a Hb in the target range. One study found less LVH *and* less EPO resistance in patients on short daily hemodialysis.¹⁶ A number of studies have also found that less EPO is needed for short daily^{17,18,19,20} or for nocturnal^{21,22,23,24} hemodialysis.

Talk with Your Doctor

EPO has been safely used to keep people on dialysis in a target Hb range of 11 to 12 g/dL for nearly 20 years—since 1989.

The Renal Physician's Association says that you and your doctor should decide how to treat your anemia.²⁵

You are the only one who can decide what you value more: your quality of life, or the chance of a risk. If there is a tradeoff to be made, you are the only one who can make it. Talk with your doctor and decide what will be best for you.

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