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F.D.A. Orders Warnings on Anemia Drugs

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<http://www.nytimes.com/2007/03/09/washington/09cnd-drug.html>

The [Food and Drug Administration](#) issued strict new warnings today about overuse of drugs for [anemia](#), following a flurry of recent studies suggesting that the medications might cause heart attacks or make [cancer](#) worse in some patients.

The agency said the warnings had been added to the labels of the drugs, and that doctors should use the lowest dose necessary to help patients avoid blood transfusions.

It also said it was re-evaluating the validity of claims that the drugs can boost energy levels or otherwise improve a patient's quality of life. Those claims are in the drugs' labels, and some have been used to advertise the products.

Almost one million Americans use one or another of the drugs, which are mainly meant to treat anemia caused by kidney disease or by cancer [chemotherapy](#). The drugs are darbepoetin alfa, sold as Aranesp by Amgen, and epoetin alfa, sold as Epogen by Amgen and as Procrit by Johnson &

Johnson.

Both drugs are genetically engineered forms of erythropoietin or epo, a substance made by the human kidney that boosts the production of hemoglobin, the compound in red blood cells that helps them ferry oxygen to the body's tissues.

Sales of the drugs totaled about \$10 billion last year, making epo the best-selling product of the biotechnology industry so far.

The drugs have been heavily advertised, and there is evidence that they have been overused, in part because kidney dialysis centers and oncologists can increase their profits by prescribing more of the drugs. The new warnings are likely to prompt many physicians to cut back on their use.

Officials of the drug agency stressed that the main safety risks of the drugs appear to occur when the drugs are used to raise hemoglobin to levels higher than 12 grams for each deciliter of blood, the level indicated in the prescribing information for the drugs.

Even then, the data showing risks are “very, very preliminary,” Dr. Patricia Keegan, director of the agency's division dealing with biotech cancer drugs, said on a

conference call with reporters today. Nevertheless, she said, the pattern in the data seemed consistent enough to merit the new warnings.

In a statement posted on its Web site, Amgen said that in the recent studies, “physicians treated patients differently than they would in standard clinical practice.” In a separate press release, the company said that the “vast majority of oncologists and nephrologists” do not appear to be using the drugs to maintain hemoglobin levels above 12 grams per deciliter.

The new warning for the drugs will be bordered by a black box, the strictest type of warning. It will include information on six studies, most of which have been made public in the last few months.

In one study, published in the [New England Journal of Medicine](#) in November, patients with kidney disease who were treated aggressively with Procrit had more heart attacks and deaths than those treated less aggressively.

One of Amgen’s own studies showed an increased death rate in cancer patients treated with Aranesp compared with those who were given a placebo. The patients receiving Aranesp were not receiving chemotherapy, and their anemia was instead presumed to have been caused by the cancer itself. That is not an approved use, but Amgen officials said it

nonetheless accounted for about 10 percent of all Aranesp prescriptions.

Anemia, a deficiency of red blood cells and hemoglobin, causes fatigue and other symptoms, like loss of concentration.

But agency officials said that the manufacturers have never demonstrated in studies that use of the drugs actually improves energy levels or quality of life when used in patients with anemia caused by chemotherapy. Rather, the drugs are approved only to reduce the need for blood transfusions.