Serious doubts surround the expensive anti-anemia drugs widely prescribed for the fatigue associated with cancer chemotherapy and kidney dialysis. They are also given to decrease the need for blood transfusions. But the latest studies show that these injectable drugs, sold under the brand names of Aranesp, Procrit and Epogen (Eprex in Canada), increase the risk of death, deep vein blood clots and heart damage. Several recent trials had to be stopped prematurely because the drugs either caused the cancer to progress more rapidly or the cancer patients to die sooner. In some trials, the harms are caused by excessively high doses.

The FDA has taken the unusual step of calling a special meeting of its Oncologic Drugs Advisory Committee to review the new data on these drugs. Aranesp, Procrit and Epogen are all versions of erythropoietin, or EPO, which is a synthetic form of a protein produced by the kidneys that stimulates production of red blood cells. EPO drugs were approved by the FDA for the treatment of anemia in patients with kidney failure and in cancer patients undergoing chemotherapy. Anemia, a deficiency of red blood cells, is a common side effect of chemotherapy, which suppresses red blood cell production. EPO drugs are good at elevating and maintaining red blood cell levels, but now their effectiveness in treating fatigue has been called into question.

Yet fatigue in cancer patients undergoing chemotherapy was the heavily advertised reason for the TV ad campaign for Procrit. If you’re over the age of 55, these ads will be quite familiar because they appeared regularly during the Network evening news and other venues likely to have an older audience. In the standard scenario for a Procrit ad, the cancer patient cannot continue the work he or she loves because chemotherapy has produced disabling fatigue. Procrit quickly turns things around, and the cancer patient is back on track enjoying life.

At a March press briefing about the new warnings to be added to the labels of all EPO drugs, the FDA’s Richard Pazdur, MD, announced that there has never been any evidence to support the claims that EPO can increase energy or ease fatigue in patients undergoing cancer chemotherapy.

EPO drugs are heavily marketed worldwide, accounting for more than $11 billion in combined sales last year. Amgen, the world’s largest biotechnology company, makes both Aranesp (the most expensive of the three EPO drugs at $1,300 to $2,000, a shot) and Epogen. Clinical trial results announced just in the last eight months alone generated enough alarm and FDA warning letters (to health professionals) to warrant the aforementioned FDA meeting this month.

Off-Label Uses Prove Deadly

These recent trials were intended to expand the market for EPO drugs for uses beyond those initially proven according to FDA pre-approval requirements. Off-label use, as it is known in FDAspeak, refers to the prescribing of a drug for an unproven indication—a common, though questionable, practice. EPO drugs, for example, are already prescribed off-label to treat anemia unrelated to chemotherapy. (Anemia can be caused by chemotherapy or the cancer itself.) It is in a drug company’s interest (sometimes) to prove an off-label use in a clinical trial because that would allow it to openly and aggressively promote the use to doctors and the public; expand the market; and make more money.

Unfortunately, the newer trials testing off-label uses have produced disastrous results. In January, Amgen reported preliminary results from a large randomized trial that found Aranesp hastened death by 23%. The 851 participants were anemic cancer
patients not currently under treatment with either chemotherapy or radiation. There were 250 deaths in the Aranesp group and 215 in the placebo group.

Another trial, conducted last year in Denmark, showed that cancer progressed sooner in the Aranesp-treated study participants undergoing radiation therapy for advanced head and neck cancers. Amgen failed to publicly disclose that this long-awaited Danish trial was stopped prematurely last fall. In February, the Journal of Clinical Oncology published an online paper about a Canadian trial in which 70 lung cancer patients on Eprex (Epogen in the U.S.) were dying sooner. Most of the participants were not receiving chemotherapy.

These recent trials are not the first to show deadly EPO-induced harms for off-label uses. The first hint that EPO causes cancer to progress faster showed up in a 2003 German trial testing whether the drug enhances the effects of radiation therapy. The next year, a trial of women with metastasized breast cancer was stopped after four months when a higher rate of death and fatal “thrombotic events” was shown in those on Epogen and chemotherapy compared to those on chemotherapy alone. This trial was testing two off-label uses: 1) higher than normal doses of EPO; 2) in patients who weren’t anemic.

Bottom Line

All EPO trials will be reviewed this month by the FDA, which will likely generate new prescribing guidelines. The newly revised warning labels now tell doctors to use the lowest doses needed to avoid blood transfusions. Potentially fatal deep-vein blood clots and heart problems appear to be related to the administration of EPO in excessively high doses. These drugs were originally introduced to reduce blood transfusions, a procedure that was riskier in the early years of EPO use (early 1990s) than it is today.

To access the newly revised warning labels for EPO drugs on the Internet, type the words label Aranesp or label Procrit into the search box. These 22- to 42-page documents start with the new warnings to doctors. The Aranesp label describes some of the trials that had to be stopped prematurely.
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