

Counterfeit epoetin alfa products

Cara C. Tigue, BA,¹ and Charles L. Bennett, MD, PhD, MPP^{1,2}

¹ Feinberg School of Medicine, Robert H. Lurie Comprehensive Cancer Center of Northwestern University, VA

^{1,2} VA Midwest Center for Health Services and Policy Research, VA Chicago Healthcare System, Chicago, IL

This new feature is designed to help protect your patients with updates on adverse events related to various cancer treatments.

Between 1998 and 2005, the US Food and Drug Administration (FDA) received nine reports concerned with the distribution of counterfeit Epogen or Procrit, the largest number of related reports for one specific drug class. In 2002 alone, investigators discovered that several thousand patients had received vials of counterfeit Procrit and Epogen. These counterfeits remain a threat to patient safety.

The toxicity

Two clinical cases of adverse events associated with counterfeit Epogen and Procrit have been investigated. One case was a 16-year-old liver transplant recipient whose pretransplant hemoglobin level was 11 g/dL. After surgery, he received 10,000 U of epoetin alfa daily and his hemoglobin level rose to 10 g/dL by the time of discharge. As an outpatient, he continued to receive 10,000 U of Epogen weekly, but his hemoglobin level fell to 8 g/dL. Physicians increased the dosage of epoetin alfa to 40,000 U weekly using Epogen obtained from a

CVS Pharmacy. However, the patient reported muscle spasms after each Epogen injection, while his hemoglobin levels remained anemic. After 8 weeks, the CVS Pharmacy notified the patient that Amgen had issued a warning letter¹ describing counterfeit 2,000 U/mL Epogen vials that were “uplabeled,” or fraudulently relabeled, as 40,000 U/mL vials to be sold at a higher price.²

In the second case, a 61-year-old breast cancer patient was treated with radiation and chemotherapy prior to undergoing a mastectomy. She developed chemotherapy-associated anemia postoperatively that was resolved with weekly 40,000-U injections of epoetin alfa. However, she developed fatigue and mild anemia over an 8-week period during which she received uplabeled Procrit vials. The patient’s nurse then read a warning letter from Johnson & Johnson advising healthcare professionals that uplabeled vials of Procrit had been identified.³ The nurse matched the lot number and typing imperfections on one of the patient’s Procrit vials to those reported for the uplabeled Procrit vials described in the warning letter.

Where reported

After Amgen and Johnson & Johnson issued warning letters about counterfeit Epogen and Procrit, the two companies and the FDA received calls from pharmacies, hospitals, and patients that led to the determination of the likely route by which the counterfeit drugs had reached patients. Amgen and OrthoBiotech sold 2,000 U/mL vials of Epogen and Procrit, respectively, to Cardinal and Amerisource Bergen, who sold the products to a Miami pharmacy

called J&M Pharmacare. The pharmacy resold the vials to an alleged counterfeiter, who relabeled the vials as 40,000 U/mL and sold them to several regional wholesalers. One wholesaler in Phoenix sold the uplabeled vials back to Amerisource Bergen who then sold them to a CVS Pharmacy in New York, where the liver transplant recipient received them.² Amerisource Bergen also sold uplabeled Procrit vials to wholesalers in Texas, Florida, Tennessee, and New York, who then sold these vials to a regional wholesaler in Arizona. Some of these vials were subsequently sold to a local pharmacy in Missouri, where they were purchased by the breast cancer patient.

Actions taken

In 2002, a Florida state prosecutor formed an investigative group called Operation Stone Cold to coordinate the investigation of counterfeit Epogen and Procrit. In 2003, a Florida Grand Jury indicted 18 co-conspirators, 16 of whom pleaded guilty to criminal charges, and the two leaders are in jail awaiting trial. Also in 2002, Amgen and Johnson & Johnson issued a series of “Dear Health Care Professional” letters about potential counterfeit epoetin alfa products. Both companies added anti-counterfeiting information to their Web sites and fielded hundreds of calls from healthcare professionals on the subject. Johnson & Johnson also placed polychromatic seals on flaps of 40,000 U Procrit cartons.

However, a convoluted distribution system is the most important factor behind the increase in counterfeit pharmaceuticals. To prevent the selling of discounted drugs to secondary wholesalers, California, Indiana, Nevada, and

Fast Facts

EPOETIN ALFA

Erythropoietins are used to treat anemia secondary to cancer, chemotherapy, kidney disease, and HIV infection. Erythropoietin is an acidic glycoprotein hormone that stimulates red blood cell (RBC) production by binding to receptors on RBC precursor cells in the bone marrow. Two of the most common commercially available epoetin alfa formulations are Epogen, marketed by Amgen, and Procrit, marketed by Johnson & Johnson through an agreement with Amgen.

Florida have passed laws supporting mandatory pedigrees and radiofrequency identification tags for pharmaceutical products. Florida now has licensure requirements for all wholesale distributors, including criminal background checks, pedigree requirements, and greatly increased criminal penalties for counterfeiting. The FDA's Counterfeit Drug Task Force outlined several anti-counterfeiting recommendations⁴⁻⁶ and has focused pedigree enforcement efforts on pharmaceuticals most likely to be counterfeited, including the cancer drugs Lupron (leuprolide), Neupogen (filgrastim), Zofran (ondansetron), and Zoladex (goserelin).

Recommendations

The FDA's MedWatch database shows increasing reports of "loss of epoetin efficacy." As counterfeit epoetin alfa continues to threaten patient safety, oncologists should be aware that most patients who receive counterfeit pharma-

ceuticals present with a loss of clinical efficacy. In such instances, these cases should be reported to the FDA using the classification of "suspected counterfeit drug" on the MedWatch forms.⁷

References

1. 2002 Safety Alert—Epoen (epoetin alfa). Important drug warning: counterfeiting of Epoen. MedWatch: the FDA Safety Information and Adverse Event Reporting System. May 8, 2002. Available at: <http://www.fda.gov/medwatch/SAFETY/2002/epogen.htm>. Accessed October 31, 2006.
2. Eban K. Dangerous doses: how counterfeiters are contaminating America's drug supply. New York: Harcourt Incorporated. 2005.
3. 2002 Safety Alert—Procrit (epoetin alfa). Important drug warning: counterfeiting of Procrit. MedWatch: the FDA Safety Information and Adverse Event Reporting System. June 6, 2002. Available at: <http://www.fda.gov/medwatch/SAFETY/2002/procrit.htm>. Accessed October 31, 2006.
4. FDA's Counterfeit Drug Taskforce Interim Report. US Department of Health and Human Services: Food and Drug Administration. Rockville, MD: October 2003. Available at: http://www.fda.gov/oc/initiatives/counterfeit/report/interim_report.html. Accessed October 31, 2006.
5. Combating counterfeit drugs: a report of the Food and Drug Administration. US

Department of Health and Human Services: Food and Drug Administration. Rockville, MD: February 2004. Available at: http://www.fda.gov/oc/initiatives/counterfeit/report02_04.html. Accessed October 31, 2006.

6. Combating counterfeit drugs: a report of the Food and Drug Administration Annual Update. US Department of Health and Human Services: Food and Drug Administration. Rockville, MD: May 18, 2005. Available at: <http://www.fda.gov/oc/initiatives/counterfeit/update2005.html>. Accessed October 31, 2006.

7. MedWatch Online Voluntary Reporting Form (3500). US Department of Health and Human Services: Food and Drug Administration. Available at: <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>. Accessed October 31, 2006.

Ms. Tigue is Project Coordinator, Division of Hematology/Oncology, Feinberg School of Medicine, Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL. Dr. Bennett is Associate Director at VA Midwest Center for Health Services and Policy Research, Chicago, IL. He is also affiliated with VA Chicago Healthcare System; Division of Hematology/Oncology, Feinberg School of Medicine, Robert H. Lurie Comprehensive Cancer Center of Northwestern University; Chicago, IL. He can be reached at cbenne@northwestern.