Deaths Again Prompt Mifepristone Label Change

BY SHARON WORCESTER
Southeast Bureau

Clostridium sordellii has been confirmed as the cause of sepsis in four women who died in the United States following the use of Mifeprex (mifepristone) for medical abortion, the Food and Drug Administration reported.

The product's package insert—and a related public health advisory released in July after two of the cases were confirmed to be due to *C. sordellii*—have been updated to reflect the new information. The updates also note that FDA tests of manufacturing lots of mifepristone and misoprostol, which is used along with mifepristone for medical abortion, showed no signs of contamination with the bacteria.

The deaths occurred in California between Sept. 2003 and June 2005. All followed the off-label use of oral mifepristone and vaginal misoprostol given as 200 mg mifepristone orally followed the next day by 800 mcg misoprostol inserted vaginally, rather than the FDA-approved regimen of 600 mg of oral mifepristone followed by 400 mcg of oral misoprostol. An additional death in Canada in 2001 also was linked with *C. sordellii* infection following medical abortion with the off-label regimen of oral mifepristone followed by vaginal misoprostol.

The absence of any evidence of product contamination with *C. sordellii* provides support for some experts' belief that mifepristone alters innate immunity, predisposing recipients to potentially lethal infections. This theoretical mechanism of mifepristone-induced sepsis remains under investigation, but the FDA's advisory warns health care providers and patients of the potential risks of Mifeprex use.

Sepsis is a known risk associated with any type of abortion. The presentation in the cases for which medical information is available was not typical, however, according to the FDA.

"All providers of medical abortion and [emergency department] health care providers should investigate the possibility of sepsis in patients who are undergoing medical abortion and present with nausea, vomiting, or diarrhea and weakness with or without abdominal pain, and without fever or other signs of infection more than 24 hours after taking misoprostol," the advisory states.

A complete blood count should be considered in these patients, and immediate antibiotic treatment that includes coverage for *C. sordellii* is recommended if infection is suspected.

Danco Laboratories LLC did not immediately respond to a request for comment from this newspaper regarding the recent update to the Mifeprex labeling, but following the labeling change and FDA advisory in July, the company released a statement noting that Mifeprex has been used by more than 460,000 women since its approval in 2000. ■

Epstein-Barr Virus Poses Little Threat to Fetus

ST. PETE BEACH, FLA. — Maternal infection with the Epstein-Barr virus does not appear to represent a major teratogenic risk, Meytal Avgil, M.D., reported at the annual meeting of the Teratology Society.

The herpes virus—and the cause of infectious mononucleosis—has not been well studied in pregnancy, but in a recent prospective study, the rate of major anomalies was 5% in a group of more than 200 EBV-exposed pregnancies, and 3% in a group of nearly 1,200 controls. The difference between groups was not statistically significant, and the rates were within the expected baseline risk for the general population, said Dr. Avgil of Hebrew University, Jerusalem.

Furthermore, the anomalies did not follow any specific pattern in the EBV group, and were similar in the two groups, she noted.

There also were no differences in the rate of live births, miscarriages, or elective terminations of pregnancy between the two groups; the median birth weight of infants was similar in both groups, ranging from about 3,200 g to 3,300 g. The median gestational age at delivery was 40 weeks in both groups.

—Sharon Worcester

Pages 46a—46f