



DANCO LABORATORIES

PO Box 4816
New York, NY 10185

infoline

1.877.4.EARLY OPTION

www.earlyoptionpill.com

November 12, 2004

Dear Emergency Room Director:

Danco Laboratories is providing this information to assist you in taking care of patients who may present in an emergency room setting following treatment with Mifeprex[®] (mifepristone) and misoprostol. In particular, you should be aware of the rare events – serious infection, prolonged heavy bleeding and ruptured ectopic pregnancy – discussed below. From September 2000, when Mifeprex[®] was approved in the United States for marketing, through September 2004, approximately 360,000 women have been treated with Mifeprex in the U.S.

The Mifeprex treatment, Mifeprex followed by misoprostol, is indicated for non-surgical abortion in patients who are ≤ 49 days pregnant, dated from the first day of the last menstrual period (LMP). Medical abortion with Mifeprex and misoprostol presents no differently from a spontaneous abortion, with bleeding and cramping expected in the hours after taking misoprostol. In clinical trials, Mifeprex was highly effective, with a 92-95% success rate in women who were ≤ 49 days pregnant. The remainder have a surgical termination for various reasons, including ongoing pregnancy, incomplete abortion, bleeding and patient request; the vast majority of these women are treated by the physician who initially provided the Mifeprex treatment or by referral to a colleague.

However, there may be some women who present to an emergency room with serious and sometimes fatal infections and bleeding that occur rarely following spontaneous (miscarriage), surgical and medical abortions, including following Mifeprex use, and childbirth. A high index of suspicion is needed for timely diagnosis and intervention in these patients. Danco Laboratories has updated the BOXED WARNING and WARNINGS sections of the Prescribing Information as well as the MEDICATION GUIDE and the PATIENT AGREEMENT to provide information about these topics. Additional information is provided on ectopic pregnancy, which is a contraindication for Mifeprex (see WARNINGS).

Copies of the updated Prescribing Information, which includes the MEDICATION GUIDE and the PATIENT AGREEMENT, are enclosed, and it is important for you to read them carefully. A summary of the updated warnings follows:

Infection and Sepsis

In postmarketing experience following the use of Mifeprex and misoprostol, we have received a few reports of cases of serious bacterial infection, including very rare cases of fatal septic shock (see WARNINGS). No causal relationship between these events and the use of Mifeprex and misoprostol has been established. Although infection following medical abortion is rare, we ask that you be alert to the possibility of infection in your patients. In particular, a sustained fever of 100.4 degrees Fahrenheit or higher, severe abdominal pain, or pelvic tenderness in the days after taking Mifeprex and misoprostol may be an indication of infection. Atypical presentations of serious infection and sepsis, without fever, severe abdominal pain, or pelvic tenderness, but with significant leukocytosis, tachycardia, or hemoconcentration can occur.

Vaginal Bleeding

Vaginal bleeding occurs in almost all patients during the treatment procedure (see WARNINGS). According to data from the U.S. and French trials, women should expect to

* Mifeprex is a registered trademark of Danco Laboratories, LLC.

experience vaginal bleeding or spotting for an average of nine to 16 days, while up to 8% of all subjects may experience some type of bleeding for 30 days or more. Prolonged heavy bleeding (soaking through two thick full-size sanitary pads per hour for two consecutive hours) may be a sign of incomplete abortion or other complications and prompt medical or surgical intervention may be needed to prevent the development of hypovolemic shock. Patients should be counseled to seek immediate medical attention if they experience prolonged heavy vaginal bleeding following a medical abortion. Excessive vaginal bleeding usually requires treatment by uterotonics, vasoconstrictor drugs, curettage, administration of saline infusions, and/or blood transfusions.

Ectopic Pregnancy

Additionally, in postmarketing experience we have received a small number of reports of ruptured ectopic pregnancy. No causal relationship between these events and Mifeprex and misoprostol has been established. Mifeprex is contraindicated in patients with a confirmed or suspected ectopic pregnancy since Mifeprex is not effective for terminating these pregnancies (see CONTRAINDICATIONS). Physicians should remain alert to the possibility that a patient who is undergoing a medical abortion could have an undiagnosed ectopic pregnancy since some of the expected symptoms of a medical abortion may be similar to those of a ruptured ectopic pregnancy. The presence of an ectopic pregnancy may have been missed even if the patient underwent ultrasonography prior to being prescribed Mifeprex.

The MEDICATION GUIDE and PATIENT AGREEMENT have also been updated to reflect the new safety information. Each patient should have received a MEDICATION GUIDE from her health care provider before taking Mifeprex and been advised to take her MEDICATION GUIDE with her if she visits an emergency room, so that you will be aware that the patient is undergoing a medical abortion.

Abortion, whether medical or surgical, is “generally very safe and is therefore infrequently associated with complications”.¹ However, we thought that the enclosed recent publication, Phillip G. Stubblefield, MD and Lynn Borgatta, MD, “Complications of Induced Abortion” in *Obstetric & Gynecologic Emergencies Diagnosis and Management* (New York: McGraw-Hill, 2004), 65-86, may be helpful to you in your practice as it includes information on the diagnosis and treatment of possible complications following abortion, including infection and ectopic pregnancy.

The safety and efficacy of Mifeprex and misoprostol were well established in clinical trials reviewed by the FDA. The overall safety and efficacy profile remains unchanged.

We rely on medical feedback from health care professionals and therefore remind you to report serious adverse events and any on-going pregnancies following treatment with the Mifeprex regimen to us. Please provide a brief clinical synopsis (by postal mail, email or phone):

Medical Director
Danco Laboratories, LLC
P.O. Box 4816
New York, NY 10185
Medicaldirector@earlyoptionpill.com
Toll free at 1-877-4-Early Option (1-877-432-7596)

¹ Phillip G. Stubblefield, MD and Lynn Borgatta, MD, “Complications of Induced Abortion” in *Obstetric & Gynecologic Emergencies Diagnosis and Management* (New York: McGraw-Hill, 2004), 65-86.

For more information on Mifeprex, please visit www.earlyoptionpill.com or call our 24-hour toll free number at 1-877-4-Early Option (1-877-432-7596). If you have an urgent question, a physician will usually return your call within the hour. For general questions, our Medical Director typically returns calls within 24 hours.

Sincerely,
Danco Laboratories, LLC

Enclosures