PROVIDING EARLY OPTIONS

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Medical Abortion Education Initiative

FDA Announces Mifepristone Labeling Change

On November 15, 2004, the FDA announced changes to the labeling, Patient Agreement, and Medication Guide for Mifeprex®. The updated documents are available on Danco Laboratories' website at *www.earlyoptionpill.com*. The changes in the "Black Box" and the "Warnings" section of the labeling include updated safety information about infection and sepsis, bleeding, and ectopic pregnancy.

Regarding infection, the new labeling states that serious bacterial infection and sepsis can occur very rarely after spontaneous, surgical, or medical abortion. It outlines symptoms of infection and also states that "[a]typical presentations of serious infection and sepsis, without fever, severe abdominal pain, or pelvic tenderness, but with significant leukocytosis, tachycardia, or hemoconcentration can occur." Importantly the labeling clarifies that no causal relationship between the use of Mifeprex® and misoprostol and cases of serious bacterial infection and fatal septic shock has been established.

The information about heavy vaginal bleeding specifies that soaking through two thick full-size sanitary pads per hour for two consecutive hours may be a sign of incomplete abortion or other complication and may warrant medical or surgical intervention. Regarding ectopic pregnancy, the new labeling reiterates that Mifeprex® is contraindicated in patients with confirmed or suspected ectopic pregnancy. Further, some symptoms of medical abortion may be similar to those of a ruptured ectopic pregnancy and clinicians should be alert to the possibility of ectopic pregnancy, even if the patient had a pre-treatment ultrasound.

The revised Patient Agreement is very similar to the original, but specifies symptoms that warrant a call to the provider and instructs patients to take the Medication Guide with them if they seek treatment at an Emergency Room or from another provider. The Medication Guide has been reworked so the section entitled "What is the most important information I should know about Mifeprex" includes information about incidence and warning signs of infection and heavy bleeding.

In conjunction with the labeling changes, Danco Laboratories sent a Dear Health Care Professional letter and a letter to Emergency Room Directors to provide information to assist them in treating patients seeking abortion with Mifeprex® or follow-up care after using Mifeprex®. These letters are also available on the Danco website. Each Mifeprex® customer also received a mailing from Danco Laboratories that included the updated Prescribing Information in booklet form, the Dear Health Care Provider letter, and an educational chapter called "Complications of Induced Abortion" (Stubblefield and Borgatta) from a leading text book, *Obstetric & Gynecologic Emergencies Diagnosis and Management* (New York: McGraw-Hill, 2004, pp. 65-86).

The website for the U.S. Food and Drug Administration's Center for Drug Evaluation and Research includes numerous documents related to mifepristone's labeling, use, and safety, including a Mifepristone Questions and Answers document dated November 16, 2004 related specifically to the labeling changes. These may be accessed at *http://www.fda.gov/cder/drug/infopage/mifepristone/default.htm*.

The updated Medication Guides and Patient Agreements began shipping with supplies of Mifeprex® in January. As in the past, four (4) English Medication Guides are automatically included with each box of pills shipped to the provider. The new Medication Guides are easy to distinguish from the original ones since they are purple and light green and the original Medication Guides were gray. The revision date (Rev 1: 11/15/04) is also included on the last page of the new Medication Guides. Packages of Mifeprex® now shipping from the distributor include the revised Prescribing Information package insert.

**THIS IS OUR FINAL ISSUE OF *PROVIDING EARLY OPTIONS*.
SIGN UP ONLINE TO STAY INFORMED!**

This is our last issue of *Providing Early Options*. If you'd like to keep informed on medical abortion information and resources, subscribe to our Early Options medical abortion e-newsletters. These e-newsletters are sent every other month and include updates on clinical practice and research, legislative issues, patient and provider resources, and news items about medical abortion. Sign up to receive bimonthly e-newsletters at *http://www.prochoice.org/pubs_research/publications/newsletters.html*. This webpage also includes archived issues of *Providing Early Options*.

Inside This Issue

NAF Updates Protocol for Mifepristone/Misoprostol in Early Abortion

The National Abortion Federation has issued a revised protocol for early abortion with mifepristone and misoprostol. The protocol, dated February 2005, has been updated to include new data on an additional evidence-based alternative regimen option and to ensure that the eligibility, counseling, and conclusion of treatment information reflects current published literature and medical practices. This protocol replaces the previous version of the NAF mifepristone/misoprostol protocol dated October 2002.

Some of the specific revisions contained in the revised February 2005 protocol are:

1) additional information about breastfeeding after the use of mifepristone and misoprostol;
2) an additional option of administering 800 mcg vaginal misoprostol as early as 6 hours after 200 mg mifepristone. The previous protocol included the option of administering 800 mcg vaginal misoprostol as early as 24 hours after mifepristone;
3) a table, reprinted below, that provides a side-by-side comparison of the FDA-approved regimen and evidence-based alternative regimens; and
4) references to support the additional alternative regimen.

This updated protocol and numerous other medical abortion resources are available for download on NAF's website at *www.prochoice.org/pubs_research/publications/downloads/index.html.*

	FDA-Approved Regimen	Evidence-Based Alternative Regimens
Mifepristone dose	600 mg (three 200 mg tablets)	200 mg (one 200 mg tablet)
Misoprostol dose	400 mcg orally	800 mcg vaginally
When misoprostol taken	48 hours after mifepristone	6-72 hours after mifepristone ≤56 days gestation 6-48 hours after mifepristone ≤63 days gestation
Where misoprostol taken	At the medical office	At home
Gestational age limit	49 days gestation	63 days gestation
Timing of initial follow-up examination	Approximately day 14	From approximately day 4-14 ONLY in studies using 800 mcg VAGINAL misoprostol

Early Options Medical Abortion Educational Slide Program NEWLY UPDATED

NAF's series of four PowerPoint slide presentations on early medical abortion and vacuum aspiration have recently been updated to include current statistics and published research. The modules review data and essential points for the provision of medical abortion, including regimens, counseling, patient management, and administrative issues. Additionally, one module focuses on early vacuum aspiration, both as a primary method of abortion and as a back-up for medical abortion. These presentations are available free for downloading on the NAF website and can be used for staff training and in educational settings, such as medical schools and for grand rounds. The program includes the following presentations:

- Overview of Medical Abortion: Clinical and Practice Issues
- Medical Abortion Regimens
- Expected Side Effects and Management of Complications in Medical Abortion
- Early Vacuum Aspiration: An Alternative to and Back-Up for Medical Abortion

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The National Abortion Federation (NAF) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians.

naf NATIONAL ABORTION FEDERATION

NAF is the professional association of abortion providers in the US and Canada. We serve those who make choice a reality: physicians, nurses, counselors, administrators, advanced practice clinicians, and other health care professionals at medical facilities and offices in 48 states, the District of Columbia, Puerto Rico, and eight Canadian provinces. NAF is unique among reproductive health care organizations in that our mission is focused specifically on keeping abortion safe, legal, and accessible.

Values Clarification for Health Care Professionals: One Step in Successfully Integrating Abortion Services into Your Practice

For many health care professionals, the availability of medical abortion presents them for the first time with the opportunity to integrate abortion services into their practices. This may be because they are not trained in vacuum aspiration and therefore were not able to offer abortion care when vacuum aspiration was the only first trimester abortion option. Or it may be because in some states medical abortion falls within the scope of practice of some advanced practice nurses and physician assistants whereas vacuum aspiration may not or may be unclear. Or it simply may be because for whatever reason working out the logistics of providing vacuum aspiration was not possible and integrating medical abortion is more feasible.

In any of these cases, successfully integrating abortion services into one's practice may require addressing one's personal values, and those of all staff, about pregnancy options, abortion, and providing abortion services. The National Abortion Federation has published a new resource, *The Abortion Option: A Values Clarification Guide for Health Care Professionals*, with exercises designed to help health care professionals to clarify their personal values about pregnancy options and abortion, and to think about those values in the context of their professional roles and responsibilities. This guide can be used by individuals or in groups and is appropriate for the wide range of health care professionals who provide care to women experiencing unintended pregnancies. It is a valuable tool for staff training, both for new staff and for continued professional development with seasoned staff or to address particular issues that may emerge with staff. It can also be used for outreach with social service agencies, medical or other health profession schools, medical practices, and many other organizations or professionals in the community.

The guide is available free for downloading on the NAF website at *http://www.prochoice.org/pubs_research/publications/downloads/professional_education/abortion_option.pdf.*

Upcoming NAF Meetings

2005 Risk Management Seminar

The National Abortion Federation's 2005 Risk Management Seminar will be held in September this year. Program information will be available in June. To request information and to register contact NAF's Training & Education Coordinator at 202-667-5881.

30th Annual Meeting: Call for Session Proposals, Scientific Paper Abstracts

The National Abortion Federation invites session proposals and scientific paper abstracts for presentation at our 30th Annual Meeting to be held in the Spring of 2006. The deadline for session proposals is August 29, 2005 and the scientific paper abstract deadline is January 23, 2006. For more information on how to make your submission, contact NAF's Training & Education Coordinator at the phone number listed above.

The NAF Hotline

Need a source of referrals to quality abortion providers? Are you unsure if medical abortion is available in your area? Are you working with a patient who is struggling to pay for the services she needs? The NAF Hotline is the only national toll-free source of information about abortion.

We provide callers with unbiased, factual information about abortion in both English and Spanish. We receive over 3,000 calls a month from women, their partners, families, friends, and health care and social service professionals.

The Hotline offers:

- Factual information about pregnancy and abortion
- Confidential, non-judgmental support
- Referrals to quality abortion providers in the caller's area
- Referrals to funding sources
- Help in understanding state abortion restrictions
- Case management for women in difficult situations

People who call the NAF Hotline come from various backgrounds and situations. We are here to offer our assistance and resources because we believe all women should be treated with dignity and given the respect their individual situations deserve.

The Hotline is staffed 8AM to 9PM Eastern time Monday through Friday and 9AM to 5PM on Saturdays and can be reached at 800-772-9100.

Recent Studies and Journal Articles

There is an enormous amount of research ongoing about medical abortion protocols and medical abortion service delivery. Below are summaries of some recent studies. In addition to these already published studies and articles, the upcoming September 2005 issue of *Contraception* will include an analysis of the outcomes, safety, and efficacy of tens of thousands of medical abortions provided at Planned Parenthood sites throughout the U.S. since mifepristone's approval.

Cowett AA, Cohen LS, Lichtenberg ES, Stika CS. Ultrasound evaluation of the endometrium after medical termination of pregnancy. *Obstet Gynecol* 2004; 103 (5 Pt 1): 871-5.

The ultrasound finding of a thickened endometrium after medical abortion is normal. However, for clinicians used to seeing a thin stripe after vacuum aspiration, there can be a learning curve as they begin offering medical abortion services and evaluating post-medical abortion ultrasounds. This study involved a chart review of patients during a 13-month period who had undergone medical abortion to assess whether ultrasonographic findings at the follow-up visit were predictive of the need for clinical interventions. The medical abortion regimen was 200 mg mifepristone followed 24-72 hours later by 800 mcg vaginal misoprostol through 63 days gestation. The researchers identified 525 patients who returned for a post-medical abortion ultrasound within 17 days of initiation of mifepristone, and in 437 of these cases the ultrasound had a measurable endometrial thickness. The mean endometrial thickness at this follow-up visit was 4.10 +/- 1.80mm with a range of 0.67-13.4mm. There was no correlation between the gestational age at the initiation of treatment and endometrial thickness at follow-up. As expected, endometrial thickness was inversely proportional to the number of days that had passed between the initiation of the medical abortion and the ultrasound ($r=-0.22$, $p<0.001$). Researchers found a thicker endometrium in women with a failed medical abortion* compared with those who had a successful medical abortion (6.15 +/- 1.95mm vs 4.01 +/- 1.75, $p<0.001$). However, the wide overlapping range in the endometrial thicknesses in these two groups (3.35-10.0mm for failed and 0.67-13.4mm for successful) "nullified the clinical usefulness of this difference."

Using a receiver operating characteristic curve, the researchers further analyzed possible cutoff points for endometrial thicknesses at which one might institute universal treatment and found there was no acceptable point at which false-positive and false-negative rates are minimized. While both the presence of a fluid interface (noted in 6.8% of all cases) and complex echoes (noted in 17.6% of all cases) on the follow-up ultrasound were significantly associated with the need for further intervention, this significance disappeared in a multivariable analysis, leading the researchers to conclude that these parameters alone should not be used outside of the overall clinical assessment to determine the course of treatment. As laid out in the study protocol, all women whose follow-up ultrasound revealed a persistent gestational sac were treated with additional misoprostol so by protocol convention this finding was universally predictive of further clinical intervention.

The authors concluded "[e]ndometrial thickness after administration of a single dose of mifepristone and misoprostol for medical termination should not dictate clinical intervention. The decision to treat should be based on the presence of a persistent gestational sac or compelling clinical signs and symptoms."

* In this study, failed medical abortion was defined as any case in which additional dose(s) of misoprostol and/or vacuum aspiration were needed. This is a broader definition than is used in most medical abortion studies, which generally specify that a failed medical abortion is one that requires surgical intervention. However it is a reasonable definition in this case given that the goal of the study was to assess ultrasonographic findings that would predict the need for either additional misoprostol or vacuum aspiration.

Leeman L, Espey E. "You can't do that 'round here": a case study of the introduction of medical abortion care at a university medical center. *Contraception* 2005; 71(2): 84-88.

An article published in the February 2005 issue of *Contraception* describes a unique and successful approach to integrating medical abortion into the clinic system of a university medical center. For the 10 years prior to mifepristone's approval, first-trimester elective abortions were unavailable at the University of New Mexico Medical Center's clinic system. Medical and surgical pregnancy terminations were performed for fetal anomalies or to protect the health of the pregnant woman and were only available in labor and delivery or the operating room.

After the FDA approved mifepristone, the faculty in the Family Medicine Department and the Obstetrics and Gynecology Department reevaluated the provision of abortion in the UNM system. They hoped that by providing training there would be an increase in the number of residents who would provide abortion services after completing training. Several important steps over the course of more than a year and a half assisted the two departments in implementing medical abortion at the UNM Medical Center's clinic system in 2002. These included:

1) having a liaison for Family Medicine and Ob/Gyn departments;

2) developing an abortion philosophy statement through a committee consisting of members from both departments;

3) getting buy-in from the Emergency Department for the use of manual vacuum aspiration in treating the few cases where medical abortion resulted in excessive or prolonged bleeding or where the medications failed to terminate the pregnancy and also for the treatment of incomplete or missed abortion; and

4) providing a forum for values clarification and conflict resolution with all staff of the Family Medicine and Ob/Gyn departments, including residents, nursing staff, and receptionists.

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After overcoming many challenges, the residency clinics of Family Medicine and Ob/Gyn have offered over 100 medical abortions. A multi-stepped approach involving physicians and staff members in various departments led to the integration of medical abortion into the UNM departmental clinics.

Murthy AS, Creinin MD, Harwood B, Schreiber C. A pilot study of mifepristone and misoprostol administered at the same time for abortion up to 49 days gestation. *Contraception* 2005; 71: 333-336.

Previous studies have shown that shortening the interval between administration of mifepristone and administration of misoprostol in medical abortion protocols can decrease the amount of time for medical abortion to occur and can increase patient acceptability of the method. This pilot study involved 40 women at 49 days gestation or less who received 200 mg mifepristone followed within 10 minutes by 800 mcg misoprostol self-administered intravaginally. All women returned for an initial follow-up visit, which included a transvaginal ultrasound, 23-25 hours after taking mifepristone/misoprostol.

By the first follow-up visit, 36 women (90%, 95% CI 80-99) had a complete expulsion of the gestational sac. The four women whose ultrasounds revealed a persistent gestational sac at this first follow-up visit received a second dose of misoprostol and three of these women had a complete medical abortion at the time of their second follow-up visit which occurred between days 14 and 20. This represents an overall success rate of 98% (95% CI 93-100). One woman had a vacuum aspiration for a persistent gestation sac at her third follow-up visit, and another, who had passed the gestational sac at her first follow-up visit, required a suction aspiration and transfusion on day 27.

Consistent with other medical abortion studies, side effects reported at the first follow-up visit included nausea (60%), vomiting (25%), warmth/chills (55%), back pain (55%), dizziness (53%), and headache (18%). 95% of the women in this pilot study who completed acceptability questionnaires would recommend the method to a friend and 84% would choose this regimen if they required another abortion in the future.

Larger studies are needed to confirm these findings and to fully evaluate the safety and efficacy of this regimen. Additionally, it would be interesting to evaluate this regimen through 63 days gestation. However, these preliminary data suggest that this regimen may be another option for administering mifepristone/misoprostol for termination of early pregnancy.

Unauthorized Mifepristone Offered Over the Internet

There have been reports of a limited number of cases of women obtaining what they believe is mifepristone through the internet. There are also documented cases of women attempting to induce abortion with misoprostol obtained through sources other than a licensed health care professional.

The only legal and safe source of mifepristone (Mifeprex®) in the U.S. is through Danco Laboratories' designated distributor. Mifeprex® is not available online. The composition of drugs mailed to women under the guise of mifepristone is unknown. The same is true of "misoprostol" or other drugs obtained from sources outside the medical community. The mifepristone information page on the FDA's website includes a warning to consumers not to buy Mifeprex® over the internet. Specifically, the FDA website states:

"You should not buy Mifeprex over the Internet because you will bypass important safeguards designed to protect your health (and the health of others). Mifeprex has special safety restrictions on how it is distributed to the public. Also, drugs purchased from foreign Internet sources are not the FDA-approved versions of the drugs, and they are not subject to FDA-regulated manufacturing controls or FDA inspection of manufacturing facilities."

Women who are in need of medical abortion services can call the NAF Hotline (800-772-9100) for referrals to quality providers offering this option.

Clinical Training Curriculum in Abortion Practice, 2nd Edition — Coming Soon!!!

This 2nd edition curriculum, based on the National Abortion Federation's *Clinical Training Curriculum in Abortion Practice* originally published in 1995, updates content from the original to reflect new data, current practices, and terminology. It also includes techniques of manual vacuum aspiration and medical abortion. NAF's abortion training curriculum contains 10 modules with a supplemental values clarification resource and the 2005 NAF *Clinical Policy Guidelines*. It provides a strong didactic framework that includes lesson plans, program-specific questions, suggested experiences, notes, references, and lecture-ready PowerPoint presentations for a series of lectures. The curriculum can be easily adapted to individual educational situations. Included in the curriculum are sections on pregnancy detection, pregnancy options and abortion counseling, indications for inpatient procedures, medical abortion, vacuum aspiration, D&E and induction procedures, pain management and management of complications, and follow-up care. The curriculum will be available free for downloading on the NAF website *(www.prochoice.org)* and will also be available for purchase on CD-ROM. If you'd like to be notified when the curriculum is available, please e-mail naf@prochoice.org with the subject line "Curriculum" and we will send you an email update.

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Keeping Abortion Safe, Legal, and Accessible

Change of Address Requested

NAF's New Website

In November, NAF launched a new and greatly expanded website at *www.prochoice.org*. Now, more than ever, it is vital that we have up-to-date information about abortion care and policy. The new NAF website enables providers and the public alike to get informed and get active.

Some of the new features of the website include:

- Medical abortion resources for health care professionals section at *www.prochoice.org/education/resources/medical.html*
- Access to extensive publications and resources on abortion care and practice at *www.prochoice.org/pubs_research/index.html*
- Dozens of resources for health care providers, women, and advocates available for download at *www.prochoice.org/pubs_research/publications/downloads/index.html*
- Expanded information for women facing an unplanned pregnancy at *www.prochoice.org/pregnant/index.html*
- Policy resources and the most up-to-date developments on the state and federal levels and in the courts at *www.prochoice.org/policy/index.html*
- Factual information that dispels the myths about abortion at *www.prochoice.org/about_abortion/index.html*

As new resources become available, such as our forthcoming second edition *Clinical Training Curriculum in Abortion Practice*, they will be highlighted and available on the website, so keep coming back to see what's new.

Please give us your feedback at *www.prochoice.org/contact.html!*