PROVIDING EARLY OPTIONS

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Mifepristone/Misoprostol Regimens: A Comparison of FDA-Approved and Evidence-Based Alternative Regimens

When the FDA approved mifepristone in combination with misoprostol for early abortion in September 2000, it approved a particular regimen outlined in the labeling and supplementary documents. This regimen dates back to clinical trials conducted in the U.S. and France and submitted to the FDA in 1996. In the four years between the submission of that clinical trial data and the FDA's approval of mifepristone, clinical trials continued, and new data was collected on the safety and efficacy of alternative mifepristone/misoprostol regimens. Thus, the FDA-approved regimen does not incorporate the most current scientific data about mifepristone regimens.

The FDA-Approved Regimen: The FDA-approved regimen involves a three-visit protocol, spanning approximately 2 weeks. At the first visit, after appropriate counseling and clinical assessment, the woman receives 600 mg of mifepristone, given orally. Two days later, the woman returns to the office. If complete abortion is not confirmed, she takes 400 µg of misoprostol orally. On approximately day 14, she returns to the office for a third visit to confirm completion of the abortion. This regimen is FDA-approved for pregnancies through 49 days' gestation.

Evidence-Based Alternative Regimens: Historically, the FDA has not attempted to regulate a clinician's exercise of medical judgment in prescribing approved drugs for off-label or alternative evidence-based uses. The FDA has recognized that alternative evidence-based use of drugs by clinicians is often appropriate and may represent the standard of practice.

The American Medical Association has estimated that 40-60% of prescriptions are for alternative evidence-based uses. There are data to support the use of several evidence-based alternative mifepristone/misoprostol regimens, and leading abortion providing organizations have incorporated these regimens into their protocols.

The National Abortion Federation (NAF) protocol includes the FDA-approved regimen, as well as these additional evidence-based alternative regimens: 1) using 200 mg rather than 600 mg mifepristone; 2) using 800 µg of vaginal misoprostol as opposed to 400 µg of misoprostol orally; 3) administering vaginal misoprostol at home rather than (*continued on page 3)*

	FDA Regimen	Evidence-Based Regimen
Mifepristone dosage	600 mg (three 200 mg tablets)	200 mg (one 200 mg tablet)
Misoprostol dosage	400 µg PO	800 µg PV
Where misoprostol taken	At medical office or clinic	At home
When misoprostol taken	Day 3	Day 2-4
Timing of initial follow-up examination	Approximately Day 14	From Day 4-14
Gestational limit	49 days LMP	Up to 63 days LMP

** Shaded areas only apply if patient uses vaginal misoprostol

INSIDE THIS ISSUE

Mifepristone in NAF Member Facilities: An Update

Prior to mifepristone's approval, there was much speculation about its potential impact on the provision of abortion services in the U.S. Now, a year and a half since it became available in November 2000, how widely accessible is it and are women choosing it?

Throughout 2001 and continuing this year, NAF has tracked the availability of mifepristone at NAF member facilities. In the first several months after availability, there was a dramatic increase in the number of NAF members providing mifepristone. In the subsequent months, the incorporation of mifepristone at the remaining NAF member facilities continued but at a slower rate. As of April 2002, approximately 69% of NAF member clinics and individual physician members in the United States are providing medical abortion.

In January of this year, we sent a survey to U.S. NAF members to ascertain specific information about their medical abortion services. Although data collection is not complete, preliminary results based on a response rate of 86% indicate that the majority of members who offer medical abortion have seen an increase in their medical abortion patient volume since initiating services and that on average nearly 30% of women eligible for a medical abortion choose that option. Higher volume clinics are more likely to have incorporated medical abortion, and nearly 30 members not currently providing medical abortion indicated that they plan to offer this service within a year. We will issue final findings of this survey when data collection is complete.

Contraception After Medical Abortion

We recently asked NAF members about their protocols for initiating a contraceptive method following medical abortion. Here are some of the most common:

- **OCP's**: A Sunday start seems to be most common, usually the Sunday after the patient takes mifepristone/misoprostol. If mifepristone is taken on a Friday or Saturday, and misoprostol is used on Sunday, then it seems most common for OCP's to be started the following Sunday
- **Depo/Lunelle:** Injections are usually offered at the follow-up visit, 1 – 2 weeks after mifepristone administration when complete abortion is confirmed
- **IUDs:** Clinicians may choose to insert an IUD during the first post-medical abortion menses or at any time they determine the uterus is clear and there is no risk of a new pregnancy.
- **Diaphragms & cervical caps:** Fitted at the follow-up visit 1 –2 weeks later.

One of the most important things about hormonal contraceptive methods after medical abortion is to ensure the patient is aware that she may not be fully protected by her contraception for the first month and to ensure she has a back up method, such as condoms. We'd love to hear from you about your protocols.

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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 8 Canadian provinces. NAF is unique among reproductive health care organizations in that our mission is focused specifically on keeping abortion safe, legal and accessible.

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requiring an office visit for misoprostol administration; 4) using 200 mg or 600 mg of mifepristone in combination with 800 µg of vaginal misoprostol through 63 days' gestation rather than limiting use through 49 days' gestation; 5) administering 800 µg of vaginal misoprostol either 1, 2, or 3 days after 200 mg mifepristone through 56 days' gestation rather than restricting misoprostol use to two days post-mifepristone; 6) following-up sooner than day 14 if ultrasound or ß-hCGs are used.

The Planned Parenthood Federation of America (PPFA) protocol similarly incorporates flexibility to use certain evidence-based alternative regimens. The standard PPFA protocol follows the FDA-approved regimen. If a PPFA affiliate is interested in offering an evidence-based alternative to the standard protocol, the affiliate can apply for a waiver. The waivers allow affiliates to 1) use 200 mg of mifepristone followed by 800 µg of vaginal misoprostol; 2) have patients self-administer vaginal misoprostol at home; 3) omit the Day 3 visit and instead check in with the patient via a telephone call on or around Day 3. Recently, PPFA's National Medical Committee approved two more waivers: 1) extending the use of the 200 mg mifepristone/800 µg vaginal misoprostol regimen through 63 days' gestation; and 2) allowing the use of the vaginal misoprostol on Day 2, 3, or 4 at ≤ 56 days' gestation and on Day 2 or 3 for 57-63 days' gestation.

Individual clinicians and practices may take a variety of approaches in writing their protocols. When mifepristone first became available, some providers felt more comfortable employing the FDA-approved regimen. Others incorporated some of the evidence-based alternative regimens, for instance 200 mg mifepristone and 800 µg vaginal misoprostol, but may not have included other evidence-based alternatives, for instance limiting the use of this mifepristone/vaginal misoprostal regimen through 49 days' gestation rather than 63 days. Still others employed the full-range of evidence-based alternatives from the start. With time and experience, some providers who may have had more conservative protocols initially have modified their protocols to include more evidence-based alternatives. NAF has written resources to aid providers in understanding the FDA's Prescriber's Agreement as it relates to the use of alternative regimens, and to guide providers in writing consent forms for use with either the FDA-approved regimen or evidence-based alternative regimens.

It is very important to note that various aspects of different evidence-based alternative regimens cannot necessarily be mixed and matched. For instance, the data supporting the administration of misoprostol on Day 2, 3, or 4 is based on the 200 mg mifepristone/800 µg *vaginal* misoprostol regimen. Similarly, extending the use of mifepristone to 63 days' gestation is only applicable to regimens employing *vaginal* misoprostol. It is not evidence-based to employ the FDA-regimen of 600 mg mifepristone/400 µg oral misoprostol through 63 days' gestation.

Possible FDA labeling changes on the horizon: The process of applying to the FDA to modify the existing labeling to include aspects of the evidence-based alternative regimens involves conducting additional FDA-approvable clinical trials and submitting the data to the FDA in a formal application. Currently, a trial is underway employing a regimen of 200 mg mifepristone followed by 400 µg of oral misoprostol administered at home. It is expected that data from this trial will be submitted to the FDA for their consideration. Although there is data that support the safety and efficacy of vaginal administration of misoprostol, any modifications to the label of mifepristone will not include this route of administration of misoprostol, since this medication is formulated for oral use, and for the FDA to consider approving it for vaginal use it would

Ask An Expert!

In our travels to conferences, trainings, and clinics throughout the country, we hear many questions from practitioners, administrators, counselors and others involved in offering medical abortion, or contemplating integrating this service into their practices. Here are the perspectives of two experienced medical abortion providers on two questions we hear time and again. Keep in mind, there are many different approaches to setting up medical abortion protocols and managing medical abortion patients, depending on your practice size and setting, your staffing, your clientele, your experience-level, and many other factors. We welcome your suggestions for an "Ask An Expert" question for our next issue.

Laura Castleman, MD, MPH *is an obstetrician/gynecologist in private practice and also is affiliated with Planned Parenthood Mid-Michigan. She participated in mifepristone clinical trials at Johns Hopkins when she was a Kenneth Ryan Fellow in Family Planning and Women's Reproductive Health, and she has served on faculty at numerous medical conferences and seminars about medical abortion.*

Beth Kruse, MS, CNM *is a women's health care provider at Aurora Medical Services in Seattle, and has been a clinical investigator for U.S. mifepristone clinical trials since 1995. She has been invited to speak both nationally and internationally on medical abortion and is a representative for Midwives for Choice.*

1. **What sort of guidelines are appropriate regarding how close a patient must live to our office in order to be eligible for an abortion with mifepristone/misoprostol?**

Laura Castleman: I do not have any such guidelines for the following reasons: 1) The chances of a true emergency occurring are slim, so having the woman live close to my clinic is just not necessary. I know many new providers are worried about acute, heavy bleeding requiring an emergent curettage, but fortunately, I just haven't seen that. The mifepristone patients I've followed have only rarely needed any intervention at all, and it's always been on a non-emergent, scheduled basis. I just haven't seen the dreaded "middle-of-the-night, needs a stat surgical evacuation for hemorrhage" case; and 2) The interventions I've had to do on my patients have taken place up to approximately 5 weeks post-mifepristone. This is consistent with the results from a study published last year which documented that curettages post-mifepristone occur in a bimodal distribution at 1 week and then again 3-5 weeks post-mifepristone (Allen RH, Westhoff C, De Nonno L, Fielding S, Schaff E. *Obstet Gynecol* 2001;98(1):101-6). Five weeks is a long time for women to have to remain in one location—many women we see may travel significant distances away from the their home during this period. This severely weakens the impact of any such restrictions. I believe it is not practical or necessary to require patients to stay within a certain range of the clinic over that five-week period. In my community, there are very few providers offering mifepristone. In my opinion, such guidelines would not enhance patient safety, but would instead only decrease access to what is a terrific option for women seeking abortion.

Beth Kruse: Our guidelines suggest that she live within a 2-hour radius from our office. This was somewhat arbitrarily chosen as being a reasonable commute for the routine follow-up visit, as well as for any additional visits to evaluate for and/or manage complications in a timely fashion. On occasion we have provided mifepristone abortions for women from further away who have agreed to either stay with friends or family in the area, or even take a hotel, with the agreement that they will not leave the area until their abortion is determined to be complete. This latter arrangement has met with a variable degree of success, and we *have* lost some patients to follow-up this way... Hopefully as mifepristone becomes more widely available and more providers become familiar with management, women who want a medical abortion will not be forced to travel far afield for the regimen, and will not have to make such onerous arrangements. As a corollary, when more providers become comfortable with MVA techniques, low-risk

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management of complications can be effected closer to her home as well, further reducing the need for such geographical restrictions to access.

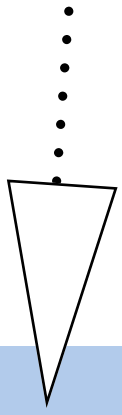
2. When is a second dose of misoprostol helpful and/or appropriate?

Laura Castleman: I do occasionally give a second dose of misoprostol. If a woman has no bleeding after her first dose of misoprostol (and I know she has an intrauterine pregnancy), I may give her a second dose of misoprostol. Also, in a woman with a persistent gestational sac, I may give a 2nd dose of misoprostol. These two applications are anecdotal, however, not based on any literature. There are mifepristone studies in which a 2nd dose of misoprostol is used (for instance, see Schaff EA, Fielding SL, Westhoff C, Ellertson C, Eisinger SH, Stadalius LS, Fuller L. *JAMA* 2000; 284(15): 1948-53). However, these studies were focusing on other issues, so whether or not a 2nd dose of misoprostol makes a difference remains an outstanding question. In mifepristone training seminars, I hear a lot of questions about whether or not a woman with a very thickened endometrial stripe on follow-up ultrasound requires repeat misoprostol. As long as the sac is no longer present on follow-up ultrasound and the patient is doing well clinically, then she is done—regardless of the amount of "stuff" in her endometrial stripe.

Beth Kruse: We typically use a second dose of misoprostol if the gestational sac is still present at the follow-up visit (day 4-15), as long as the pregnancy has been interrupted (e.g. there is no cardiac activity). This is based on our participation in the clinical trials, and also in reference to the methotrexate literature, where time to completion is discussed in reference to "either the first or second dose of misoprostol."

Anecdotally, additional doses of misoprostol often seem to be helpful, both in effecting completion of abortion and in assisting evacuation of persistent contents; we have also seen good results using it as a tool for initial triage management of excessive post-abortion bleeding.

That being said, there is actually no direct evidence that an additional dose of misoprostol is any more help than time alone would be, for either mifepristone or methotrexate abortion. In our own methotrexate guidelines, we suggest that women use a second dose of misoprostol if there has been no bleeding within 24 hours of the first dose;with mifepristone regimens, the second dose may not end up being used for as long as 12 days after the initial dose. Is there a difference in efficacy with different time intervals between doses? Between post-mifepristone and post-methotrexate misoprostol response? Between use for simple hematometra versus retained products of conception (RPOC)? The answers to these and other compelling questions lie ahead of us in the mists of research yet-to-be....



Need to find referral information for your patients?

Need someone to take time to explain parental consent laws?

Have a patient in a difficult situation and need help with case management?

CALL the NAF Hotline!

- Our toll-free hotline receives on average approximately 3,000 calls a month from women, their partners, families, friends, and healthcare providers.
- Our hotline offers referrals to quality providers in the caller's area, referrals to funding sources and offers non-biased, confidential information about abortion.
- Our hotline staff speak English and Spanish and are available to you Monday – Friday 8 am – 10 pm and Saturday and Sunday 9 am- 5 pm (EST).

The NAF Hotline is 1-800-772-9100

NAF's Quality Assessment and Improvement Program Update

After three years of operation, NAF's Quality Improvement initiative has provided NAF members with over two hundred site visits and evaluations. By the end of 2003, we will complete our first five-year round of site evaluations and will have certified all NAF member facilities according to NAF's *Clinical Policy Guidelines*, which set the standard for quality abortion care. NAF's evidence-based *CPGs* cover both surgical and medical abortion. They are based on a rigorous review of the relevant medical literature and known patient outcomes.

How the program works: Our Quality Assessment and Improvement (QAI) program is provider and patient-focused. During the site visit, NAF staff review your patient care practices according to NAF's *CPGs*, offer technical assistance on a variety of clinical or administrative issues, and work with you on the spot to resolve any deficiencies. After the site visit, your facility receives a follow-up report and a certificate that is valid for five years.

What we have learned: During the pilot phase and the first three years of operation, NAF has developed the most far-reaching QAI program for abortion providers in North America. We are thrilled to report that the vast majority of members had no significant deficiencies, attesting to the fact that NAF represents the highest quality abortion providers.

We are happy to share with you some of the findings and improvement tools that we have developed in order to help you further your goals of providing quality services to your patients. Please contact Simone Scupi, NAF's Clinical Services Director at 202.667.5881, for more information about the program.

Quality Management in the Abortion Setting

Presented as a full-day workshop at NAF's Annual Meeting in April, 2002

Presenter: Susan Edsall, a consultant specializing in long-term organizational change. Co-Facilitators: Simone Scupi, CPHQ, Deborah Van-Derhei

This workshop was developed as a pilot presentation for NAF's Regional Quality Manager Training Program, which will develop a network of local, regional, and national quality assessment and improvement specialists. NAF's new training program will begin in 2003 and will travel to different regions of the country at the request of NAF member facilities. A second quality management workshop will be held at NAF's Risk Management Seminar in September. Call NAF's Training & Education Department at 202-667-5881 for more information.

The Concepts

- Overview of current theories in healthcare quality management and their practical application in an abortion setting.
- Communication skills essential to developing your own quality program.
- The standard improvement cycle: A powerful tool to manage change, implement new services, conduct surveys and transform information into data.

The Objectives

- Understand the different philosophies of quality management.
- Identify areas for improvement and establish an action plan for implementation.
- Data Management: Apply analytic tools to measure for accountability, improvement, or research.

The Participants

- This workshop is for leaders, managers, supervisors, work teams, and individuals interested in learning how to implement quality tools in your abortion care practice.

Does your clinic need medical abortion technical assistance and training?

NAF is now offering specialized technical assistance and in-services for our members who need additional training or assistance with implementing medical abortion into your current services. *If you have a training need, please complete this form and fax it back to Deborah VanDerhei at 425-672-2598.*

Are you currently providing medical abortion? ___ yes ___ no

Our clinic could use help with the following. Rank up to five topics in order of importance (1 through 5)

____ Phone intake

____ Patient Screening

____ Counseling

____ Developing protocol

____ Managing side effects and complications

____ Arranging emergency backup

____ Ultrasound training

____ Billing and Reimbursement

____ Patient agreement/consent form

____ Legal/regulatory questions

____ Patient volume

____ Patient flow

____ Staff values clarification on medical abortion

____ MVA Training

____ On-call issues (staffing, volume, etc)

____ Other (please specify) : _____

What is Technical Assistance?

As a benefit of NAF membership, assistance and training is available to support clinics that are exploring the initiation of medical abortion services as well as those with established services. These programs can be accessed either through telephone consultation or on-site training designed specifically for your staff.

Possible areas for technical assistance and in-services:

- Developing/refining protocols
- Patient volume and/or patient flow
- Medical abortion pricing/drug costs
- Paperwork (Patient Agreement, consent forms, etc)
- After hours triaging
- Patient screening
- Billing and reimbursement
- Emergency back up
- Legal/regulatory issues
- Ultrasound training
- Phone counseling/intake
- MVA training
- Managing side effects/complications
- Buy in from Medical Director, Owner, or others
- Staff values clarification

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Keeping Abortion Safe, Legal, and Accessible

Change of Address Requested

Mailing Address Line 1
Mailing Address Line 2
Mailing Address Line 3
Mailing Address Line 4
Mailing Address Line 5

EARLY OPTIONS: EDUCATING HEALTH CARE PROFESSIONALS AND WOMEN ABOUT MEDICAL ABORTION

NAF has developed a series of multimedia resources to educate health care professionals and women about the use of mifespristone and misoprostol for early medical abortion. Topics covered include medical abortion regimens, patient management, patient counseling, the role of ultrasound and early surgical abortion in medical abortion care, legal and administrative issues, and the history of medical abortion. The following materials from the Early Options Medical Education Series are available for purchase from NAF:

- CME-Accredited Self-Study Guide for Health Care Professionals
- Early Options Educational Slide Program on CD-ROM (8 modules)
- Early Medical Abortion with Mifepristone or Methotrexate: Overview and Protocol Recommendations (NAF Curriculum Module)
- Health Care Professionals Education Video Series (5 videos)
- Training & Resource Manual (Slide Modules, Reference and Resource Materials)
- CME-Accredited CD-ROM: Managing the Virtual Patient (coming summer 2002)
- Patient Education Video and Brochure in English and Spanish

New Resources Coming Soon!

This summer an interactive CME-activity will launch on NAF's medical abortion website, www.earlyoptions.org. The program will also be available on CD ROM. This CME activity will include five modules covering the topics of medical abortion regimens, management of side effects and complications, medical abortion counseling, the role of ultrasound and laboratory testing, and administrative and regulatory issues. The program will also include case studies, video clips of expert clinicians and women who have chosen medical abortion, and interactive pop-up questions to check users' understanding of the material.

We are also translating our medical abortion patient brochure into Bosnian-Croatian, Chinese, Russian, and Vietnamese.

To order any of these materials, visit our website at www.earlyoptions.org, email us at earlyoptions@prochoice.org or call the NAF office at 202-667-5881.