

## **Mifepristone – 'RU486'**

### **Briefing paper**

#### **Reproductive Choice Australia August 2005**

#### **What is Mifepristone and how does it work?**

Mifepristone, also known as RU486, was developed in the early 1980s by the French pharmaceutical company Roussel-Uclaf and belongs to a class of compounds called antiprogestins. Antiprogestins counteract the action of the hormone progesterone.

In the early 1980s it was shown that mifepristone, when given in conjunction with prostaglandin (a drug that stimulates uterine contractions), was effective at inducing the abortion of a pregnancy of up to seven week's duration.

Mifepristone blocks the action of progesterone, which is needed to sustain a pregnancy. This results in:

- Changes in the uterine lining and detachment of the pregnancy
- Softening and opening of the cervix
- Increased uterine sensitivity to prostaglandin.

Mifepristone is used in combination with another medication - a prostaglandin analogue called misoprostol. Misoprostol causes the uterus to contract and helps the pregnancy tissue to pass.

#### **How is Mifepristone administered?**

Mifepristone is generally prescribed by a medical practitioner. A woman must visit a clinic for a physical examination and pregnancy test. Her medical history is screened to determine if there is any reason why the drug should not be used in her case. Informed consent must be obtained in relation to the termination of pregnancy and method of termination.

Mifepristone is provided in tablet form, and taken orally in the presence of a nurse or doctor before leaving the clinic. About half of the women begin to bleed the day after taking mifepristone.

In some countries where Mifepristone is available, a woman must return to the clinic after 48 hours to receive the misoprostol or other prostaglandin which will complete the abortion. The prostaglandin can be administered orally or vaginally. The woman stays at the clinic for the next 4-6 hours. Most (up to 90%) abort there; the rest will abort later at home. In other countries, the women are provided with the prostaglandin tablets to take at home.

A woman must return several days later for a physician's examination to make sure the abortion is complete and to determine if she has experienced any side effects. Bleeding, similar to a heavy period, lasts on average for 10-12 days.

It is important to note:

- Medical abortion with mifepristone/misoprostol requires at least two visits to a doctor's office or clinic.

- Approximately two-thirds of women will have a complete medical abortion within 4 hours of using the misoprostol.
- Approximately 90% of women will have a complete medical abortion within 24 hours of using the misoprostol.
- Complete abortion generally occurs more quickly when misoprostol is used vaginally rather than orally.

### **Other uses of Mifepristone:**

#### Emergency or 'post coital contraception'

In 1992, a study showed that mifepristone, when used in a lower dose than used for termination of pregnancy, was effective as a method of emergency contraception.

This study showed that mifepristone reliably prevented pregnancy when given up to 5 days after unprotected intercourse, and that its use resulted in fewer side effects than the combined emergency contraceptive regimens used at the time. Because of its effectiveness, it was used as the comparator in a landmark WHO study on emergency contraception.

#### Regular contraception

Because antiprogestins both inhibit ovulation and prevent implantation it seems there is potential to use these compounds as a regular method of oestrogen-free contraception.

Another option is the regular use of a single dose of an antiprogestin given in the early luteal phase, which offers the possibility of once a month oral contraception.

#### Controlling bleeding in those using progestogen-only contraception

Since the early 1990s there has been a marked increase in the number of long-acting progestogen-only contraceptive methods available, and in the number of women choosing to use them. Such methods include injectable contraception as well as contraceptive implants and progestogen-bearing IUDs.

A major problem with these progestogen-only contraceptive methods is that they invariably disrupt the regular menstrual cycle. Unacceptable bleeding patterns represent the most common reason for women discontinuing their use.

Preliminary studies indicate that the use of antiprogestins such as mifepristone may be effective in stabilising the uterine lining in women using progestogen-only contraceptive methods and therefore may provide a useful treatment option for women experiencing irregular bleeding while using them.

#### Non-contraceptive uses

Antiprogestins have also been used in the treatment of a variety of medical conditions that are not associated with contraception.

They have been used in the treatment of large, inoperable meningiomas and in the treatment of Cushing's Syndrome. They have also been used in the treatment of breast and prostate cancer and there are indications they may be useful in the management of glaucoma and depression.

Antiprogestins also appear to have a role in the management of several gynaecological conditions, including endometriosis, and uterine fibroids.

### **Is Mifepristone effective?**

Mifepristone is a safe and effective alternative to surgical abortion.

Mifepristone is 95% effective if taken in the first nine weeks of pregnancy, meaning that 95% of women will have a complete abortion when using mifepristone in combination with a prostaglandin (i.e. misoprostol) up to 63 days after the start of the last menstrual period. The remaining women will need a surgical abortion either because of ongoing or excessive bleeding, an incomplete abortion (tissue remains in the uterus but there is no growing embryo) or an ongoing pregnancy (a viable growing pregnancy, which occurs in less than 1% of cases).

Side effects, such as pain, cramping and vaginal bleeding, result from the abortion process itself, and are therefore expected with a medical abortion. Other side effects of the medications themselves may include nausea, vomiting, diarrhea, chills, or fever.

Complications are rare, but may include excessive vaginal bleeding requiring transfusion (occurs in approximately 1 in 500 cases), incomplete abortion or ongoing pregnancy requiring a surgical abortion.

### **Is Mifepristone safe?**

Mifepristone has been used, in combination with other medications called prostaglandins, for medical abortion since 1988 in France and China, and since the early 1990's in the United Kingdom and Sweden. It has been more recently licensed in nine other European countries and Israel. In September 2001, mifepristone was approved for distribution in New Zealand. Millions of women worldwide have safely used mifepristone regimens. Evidence suggests it carries the same risk profile as surgical abortion, which is agreed to be one of the safest and most common medical procedures.

### **Advantages of Mifepristone**

- Mifepristone can be administered to a woman as soon as she knows that she is pregnant and wants to have an abortion. By contrast, a woman must wait until the 5th/6th week before she is able to have a vacuum aspiration abortion.
- Pregnancy termination with mifepristone is non-surgical, requires no anesthesia and puts women at no risk of perforation, damage to the cervix or infection from instruments.
- Many women prefer mifepristone because it allows them greater psychological control over the termination of pregnancy. It is also considered less physically invasive and appears more similar to a miscarriage than to an induced abortion.
- Mifepristone has the potential to make abortion more accessible. Administering it does not require the same level of specialized medical expertise or time as surgical abortion. Furthermore, mifepristone should eventually be cheaper than a surgical abortion.
- In the Australian context, early medical abortion using mifepristone would make abortion services more access to women living in rural, regional and remote areas. Currently many women are required to travel long distances to capital

cities to access services. These travel and cost imposts disadvantage poor, young women and women who are sole parents.

### **Disadvantages of Mifepristone**

- Mifepristone is only effective during the earliest weeks of pregnancy, a time when some women do not yet know they are pregnant.
- Mifepristone takes longer than a surgical abortion. A vacuum aspiration abortion is done in 15 minutes, whereas mifepristone takes two days or more and, at present, requires two trips to the clinic for the abortion itself.

### **Why can't Australian women access Mifepristone?**

In June 1996, the Australian Therapeutic Goods Act 1989 was amended to introduce special procedures for drugs intended to be used to induce medical abortion. Under this amendment the Health Minister is required to approve the importation, evaluation, registration and listing of these drugs and any such ministerial approval must be tabled in both houses of parliament within 5 sitting days.

This type of restriction applies to very few therapeutic drugs. The restriction on mifepristone importation resulted from a political deal between the major political parties and an anti-choice Senator, Brian Harradine, who held the balance of power. It was not a result of concerns over the safety or efficacy of mifepristone, which has been certified by the World Health Organisation as safe and acceptable to women.

The requirement of ministerial approval continues to discourage pharmaceutical companies and organisations from applying to distribute mifepristone in Australia. As the Therapeutic Goods Administration application process works on a cost recovery basis, the expense involved for the sponsoring company can be significant. Companies are unwilling to undertake this expense for mifepristone, when the Minister may overturn the approval by the Therapeutic Goods Administration. There are no guidelines for Ministerial approval and the current Federal Minister for Health, Hon Tony Abbott MP, is anti-choice.

The restriction is contradictory on a number of fronts. Safe and legal surgical terminations are generally accessible to most Australian women. These procedures are also partially rebatable under the Federal Government's Medicare (Health Insurance) scheme.

If surgical terminations are deemed to be acceptable by our government, why not medical terminations?

### **Denying women access to Mifepristone: the moral implications**

It is not right that Australian women have been denied access to mifepristone for so long. The significant impact mifepristone can have on women's health and choices makes the drug - to quote the French Health Minister who insisted the drug become available in that country in 1988 - "the moral property of women". Its safe use by countless women across the globe disproves claims that it poses unacceptable risks. Like all drugs, women are entitled to accurate information about the risk and benefit profile of mifepristone for their particular condition, and to make an informed choice as to use.

Because clinicians who provide medical abortion have no choice but to use less effective and reliable drugs, the government's refusal to reverse the legislative impediments to the

drug's importation puts women's health at risk. Women's lack of access to a safe and reliable drug for other medical conditions also poses unacceptable risks to their health.