

RU486, or not?

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Should the 'abortion pill' be available in Australia?



RU486 or mifepristone was not invented with the intention of producing an abortifacient or abortion pill. Mifepristone would have been hailed as a medical breakthrough with broad potential if one of its many applications were not to produce abortion.

In 1980 Professor Etienne-Emile Baulieu, a medical doctor and biochemist and his team in France, synthesised mifepristone. It was one of the first of a new class of drugs – anti-progesterones. Ten years earlier, receptors had been identified in the uterus to which the hormone progesterone attaches. Mifepristone is a chemical very like progesterone. It binds to the receptor and blocks the action of progesterone.¹ These receptors are widespread in the body. They are present, for instance, in the brain and the breast as well as in the uterus. A drug which blocks the action of progesterone potentially has many applications. It can be used not just as an abortion inducer but as a contraceptive throughout the menstrual cycle. It has other obstetric and gynaecological uses such as in the induction of normal labour and the treatment of ectopic pregnancy. It can be used to treat progesterone dependent cancers in the breast and meninges – the coverings of the brain.² Mifepristone also has potential in the treatment of Cushing's syndrome – a disease caused by the overproduction of glucocorticoid hormones. Incidentally, Cushing's syndrome has many of the features of aging and so mifepristone could be used in the study of the degenerative processes associated with aging.³

However, its application as an abortifacient soon overshadowed its other potential in the political if not in the scientific arena.

Progesterone is a hormone essential for the establishment and maintenance of pregnancy. Mifepristone binds to the receptors in the uterus and blocks the action of progesterone. Without the action of progesterone the pregnancy fails. Mifepristone, taken with another drug called a prostaglandin, produces a medical, as distinct from a surgical, abortion in up to 99% of women. The few for whom complete abortion does not occur proceed to surgical abortion. Medical termination of pregnancy using mifepristone and a prostaglandin is widely practised in France, Great Britain and China. Sweden has recently authorised its use in medical abortion. Medical abortion with mifepristone/prostaglandin is accepted as safe and effective and many women who have the choice opt for the medical rather than the surgical procedure.⁴

Given this potential and the multiple other applications, why is Roussel-Uclaf, the pharmaceutical company which manufactures the drug, not actively promoting its sale – at least to the 90% of countries in the world where some sort of abortion is legal? Why is there no action planned by Roussel-Uclaf to introduce the drug to Australia?

Politics of mifepristone

As soon as the abortion-producing potential of mifepristone was recognised, anti-abortion, anti-choice movements around the world swung into political action. These organisations referred to mifepristone as 'the death pill' and 'the human pesticide'. A Vatican spokesperson said: 'Let's have the courage to say so openly – a way of killing with no risk for the assassin has finally been found'.

An Australian Right to Life spokesman said that allowing mifepristone to be marketed here would be: '... like declaring chemical warfare on the next generation of Australians'.

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Congressman Robert Dornan in the USA made repeated legislative attempts to block research on mifepristone and succeeded in obtaining a Food and Drug Administration import alert embargo. This implied to the rest of the world that the drug was dangerous.

A Texan pro-life campaigner said: 'We are of course trying to use every bit of political leverage and political clout we have to keep it (mifepristone) out of the US'.

Meantime, in France in 1988 the Health Ministry announced the approval of mifepristone as an abortifacient but shortly afterwards Roussel-Uclaf announced the suspension of marketing of the drug. This followed protests from the French Catholic church and anti-abortion groups, threats of boycott against Roussel-Uclaf and its parent company, Hoechst, and threats to the safety and lives of company employees and their families. Two days after the suspension of sales Claude Evin, the then French Minister of Health, using the economic clout of the French Government's majority share holding in Roussel-Uclaf, ordered the company to put mifepristone back on the market. He said that the drug should be made available 'in the interests of public health', that withdrawing the pill 'would deprive women of an important scientific advance' and that the drug was now 'the moral property of women' and not just the property of the drug company.

Despite this, in December 1988 Roussel-Uclaf announced the suspension of distribution of mifepristone apart from in France. This suspension included sales to China where the drug was already approved, and Great Britain, Sweden and the Netherlands where approval was imminently expected.

In February 1989 distribution of mifepristone to authorised abortion clinics in France began. In September 1989 Professor Baulieu received the Lasker Award – the most prestigious award for medical research in the USA for his part in the production of mifepristone. In November 1990 the Minister of Health in the West Australian Government banned Professor Baulieu from speaking to gynaecologists and obstetricians at a hospital in Perth. In July 1991 mifepristone was approved for use in medical abortion in Great Britain.

Although most of the protests against mifepristone have been from anti-abortion advocates, there has also been opposition from a small minority of feminists. In September 1991 a group of feminist academics from the USA and Australia published a detailed attack on the safety and desirability of medical abortion with mifepristone/prostaglandin. They claimed that the drugs were not safe, not adequately tested and that the introduction of this method of abortion would further undermine the autonomy of women.⁵

These are just some of the controversial and confusing events in the history of mifepristone. This new drug has focused international attention on the unresolved controversy about abortion and the rights of women to control their fertility.

Use in medical abortion

In France, mifepristone is authorised for use in pregnancy termination at up to seven weeks gestation and in Great Britain at up to nine weeks gestation. The woman is given mifepristone tablets and then 36-48 hours later the other drug, prostaglandin. Originally prostaglandin was administered as an injection or vaginal pessary but now a tablet form of this second drug is available.

If mifepristone is used on its own, only 80-85% of pregnancies are terminated but, in combination with a prostaglandin, 99% of women have aborted within 24 hours of prostaglandin administration. The abortion resembles a spontaneous miscarriage.

Most women find the procedure uncomfortable but acceptable and the majority of those who have the choice opt for medical rather than surgical abortion. Most women report preferring to avoid anaesthesia and surgical intervention. They feel medical abortion is less embarrassing and prefer their more active role in the procedure. They feel more in control, consider the method is more natural and dignified and feel less invaded. However, some women who have had medical abortions report that the process takes too long and they do not like to be so involved in the abortion.

Pain relief may be required and 25-33% of women have some diarrhoea, nausea or vomiting. These side effects are mainly due to the prostaglandin and with the use of newer improved prostaglandins, are reduced in incidence. Less than 1% of women require urgent surgery because of heavy bleeding. There is negligible danger of infection or cervical damage. These are small but significant risks with surgical abortion.

In April 1991 the first death associated with medical termination of pregnancy was reported. A 37-year-old French woman died from a heart attack after injection of the prostaglandin sulprostone. She had had 12 children and one previous abortion and was a heavy smoker. Since this death, medical abortion has been limited to women of less than 35 years of age who are fit and no more than light smokers.

Women occasionally die from complications of legal surgical abortion. The safety of surgical and medical methods of abortion seems to be comparable.

Women have throughout history sought oral means to terminate pregnancy. Medical abortion is a safe alternative to surgical abortion and has some advantages.

There is, however, concern that the introduction of medical abortion could result in reduced access to safe surgical abortion and that the present expertise in this area could diminish.

There is evidence that medical abortion may be significantly cheaper than surgical abortion. Cost is an important consideration in any health care system but is particularly pertinent in poorer developing countries.⁶

Medical abortion in developing countries

There is an anxiety about the developed world imposing population control methods on the developing world. There is no doubt that as women become more educated, more economically independent and more powerful they usually choose to have fewer babies. Many developing countries have access to legal abortion in some circumstances but most have a very limited number of people trained in surgical abortion procedures and most have inadequate services. Hence most of the 200,000 women dying each year from illegal abortions and the countless thousands more who are damaged by these abortions are from developing countries.

In November 1988 the Indian Council for Medical Research advocated that the introduction of mifepristone to India should be gradual, starting in experienced well-equipped centres, and that studies to address cost effectiveness, user acceptability and logistical problems should be done.⁷

However, women health workers in Bangladesh, writing about the use of mifepristone concluded that the likely disadvantages outweighed the likely benefits and that though medical abortifacients held promise, the mifepristone/prostaglandin combination was not yet suitable for introduction to countries with weak health infrastructures.⁸

China is not a signatory to international patent agreements and therefore ignored Roussel-Uclaf's ownership of mifepristone and manufactured its own. China is now using medical abortion widely and is assessing whether it is a cost-effective method for that country.

One of the problems about medical abortion in developing countries has been the availability of a suitable prostaglandin. Until recently the prostaglandins used have been expensive, administered by injection or intravaginal pessary and have required refrigeration. However, cheaper oral preparations which do not require refrigeration and have a lower incidence of side effects are now available.

Fifteen years ago the World Health Organisation stated there was a need for a safe method of medical abortion to improve maternal reproductive health on a global scale. Illegal abortion causes 13% of all maternal deaths in Sri Lanka, 25% in Nigeria and 36% in Chile. These women know the risk they take but they see no other alternative.

Other uses of mifepristone

Further applications in fertility control

Post-coital contraception has been attempted throughout history but with little success until recent times when a short course of high dose oestrogen and progestogen was found to be fairly reliable in preventing pregnancy after unprotected intercourse. Mifepristone has now been found to be a highly effective post-coital contraceptive and its administration causes significantly fewer side effects than the oestrogen/progestogen method.⁹

Researchers in Chile are investigating mifepristone as an ovulation inhibitor. They are also looking at its potential as an endometrial contraceptive. Very low doses of mifepristone seem to alter the uterus lining so that implantation of the egg does not occur – while leaving the natural ovarian and pituitary hormone output unaffected. If this proves a practical possibility it is a most exciting advance in contraception.¹⁰

Other obstetric and gynaecological uses

Mifepristone softens and dilates the cervix. It may be useful in making procedures such as colposcopy – a very common gynaecological procedure involving examination of the cervix with a microscope – and the insertion of intrauterine contraceptive devices easier and less painful.

When a foetus dies in the womb, delivery of the dead foetus is an emotionally difficult and potentially physically dangerous procedure for the woman. Mifepristone has been used to induce labour in the presence of intrauterine foetal death.¹¹

Mifepristone has also been used to terminate pregnancy in the presence of foetal abnormalities and to induce labour at the end of a normal pregnancy.

It has potential in the treatment of endometriosis which produces menstrual pain and reduces fertility in 10% of women of reproductive age, and it has potential in the treatment of fibroids as well as in the treatment of ectopic pregnancy, allowing preservation of the Fallopian tube.

Other medical applications

Mifepristone has been used in the management of hormone-dependent cancers. Patients with advanced breast cancer and inoperable meningiomas have been treated with mifepristone with some success. Other tumours including some bowel, kidney, liver and uterine cancers can show relevant hormone dependency and mifepristone may be useful in their management.

Mifepristone has possible application in the treatment of AIDS.

It is of proven use in the endocrine disease, Cushing's syndrome, and has considerable potential as a research instrument in the investigation of several disease processes including depression, obesity and hypertension.¹²

Conclusion

There is no doubt that the development of mifepristone is a major scientific breakthrough. Its wide potential would seem to make the case for increased clinical availability unassailable.

Several decades ago treatment with a drug called methotrexate was shown to cure an unusual cancer that occurs in the womb. Methotrexate also induces abortion. Methotrexate is now an essential part of several effective cancer treatments and is used in the management of other serious and debilitating diseases. If the so-called pro-life activists of the day had prevented the development and distribution of methotrexate because of its abortion producing potential, people would have been denied the benefit of a valuable and life saving drug.¹³

That is what is happening with mifepristone.

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