Mr. Elton Humphrey
Committee Secretary
Community Affairs Committee
Department of the Senate
Parliament House
Canberra, ACT

Enclosed herewith is my submission regarding the importation and use of the drug Mifepristone (RU 486). I should be grateful for the opportunity to give further contributions in person when the Senate committee conducts oral sessions in Sydney/Melbourne.

INTRODUCTION

The drug Mifepristone is a steroid derivative originally developed in the course of research looking to treat a rare hormonal disorder called 'Cushing's Syndrome', caused by an excess of the hormone Cortisol. It was quickly realised however that this compound also blocked the progesterone receptor. The French pharmaceutical company, Roussell-Uclaf, continued this line of research realising that progesterone is the 'pregnancy hormone' and that a compound which blocked this receptor would end a pregnancy.

Over the ensuing two decades however, no pharmaceutical company was prepared to produce and market this compound.

Eventually, the Population Council set up Danco Laboratories to produce and market this drug. Its production takes place in China and many believe this is, in part, to make any attempt, in the industrialised world, to litigate against the manufacturers of this drug, very difficult. It also raises concerns about the quality control of the drug.

MODE OF ACTION

The compound Mifepristone blocks the progesterone receptor. Progesterone is vital for the successful continuation of a pregnancy. In the first 8-10 weeks of the pregnancy a small area on the mother's ovary, called the corpus luteum, is responsible for the production of progesterone, but gradually the placenta assumes full production and the corpus luteum involutes.

RECOMMENDED MEDICAL REGIMEN FOR ADMINISTRATION TO END A PREGNANCY

In the United States, the FDA recommended that the drug could be used up to Day 49 of the pregnancy to induce abortion. While Mifepristone ends the pregnancy another drug must be administered to ensure that the contents of the gravid uterus are expelled. This drug, Misoprostol, a prostaglandin, is administered 48 hours after the Mifepristone. A third visit by a doctor is recommended 14 days after the administration of Mifepristone to ensure that the abortion is complete.

Both these drugs are recommended to be administered orally. A screening ultrasound is also recommended to ensure the pregnancy is intra-uterine.

REPORTED COMPLICATIONS OF THE USE OF THE MIFEPRISTONE/MISOPROSTOL REGIMEN

Under the Freedom of Information provisions in the United States, numerous adverse event reports have come into public light. As well, published reports in peer reviewed medical journals, the most recent of which appeared in the prestigious New England Journal of Medicine, have highlighted serious and sometimes fatal consequences for the women accessing these drugs.

Numerous incidents of haemorrhage have been reported, many of which have required blood transfusions, a few of which have been fatal including two deaths due to ruptured ectopic pregnancies. Neither of these women had ultrasounds performed prior to the administration of Mifepristone.

It is apparent from examining the reports that some of the more serious blood loss was related to the inability or uncertainty of the woman in being able to distinguish between ‘normal’ blood loss, about which she had been warned when signing a very long consent form and pathological loss. Since she was bleeding at home, this uncertainty, in some cases, proved fatal or near fatal.

There have been reports of women being confronted by the visibly human products of the abortion, again in the relative isolation of their home.

Sepsis has emerged as another potentially serious complication, with the New England Journal of Medicine reporting the death of five young women, three of which were due to an organism identified as part of the normal flora of the female genital tract, Clostridium Sordelli, a gram positive anaerobe.

This organism is not associated with the normal clinical indication of infection such as fever so that the associated symptoms are indistinguishable from what the patient has been warned to expect as ‘normal’ sequelae.

DIFFICULTIES IN MEDICAL SURVEILLANCE

As discussed above, the recommended regimen for the use of the drug incorporates a total of three visits to the doctor, ideally the same doctor on each occasion.

Reviewing the adverse events reported it is apparent that many doctors and clinics are not complying with this recommendation, in order to save time and money. Some doctors are omitting the second medical review preferring to give the prostaglandin to the patient at the first visit to administer to herself at home. Some women are using this drug vaginally rather than by the recommended oral route. This is postulated as one of the confronting factors in the deaths of the women from infection combined with postulated suppression of the host immune response by Mifepristone.

As a family physician, I can attest to the difficulty in getting patients to attend for all three visits. Under the HIC funded Practice Incentive Payments initiative, doctors were permitted to bill the HIC under a designated item number for an asthma management protocol, called Asthma 3, which involved three visits to the attending physician.

Most of the money designated for this chronic disease management item went unused because doctors could not persuade patients to attend for all three visits.

RECOMMENDATIONS

I would suggest that the discretion about the legal use of this compound remain with the Minister for Health and that no approval be granted. As well, the use of Misoprostol in the regimen does not conform to the approved indications for its use. This ‘off-lake’ use of this drug would have important medico-legal implications for the physician in the case of a serious adverse event.

Yours Sincerely,

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