New drugs

Mifepristone

Approved indication: termination of pregnancy
Mifepristone Linepharma (MS Health)
200 mg tablets
Australian Medicines Handbook Appendix A

Mifepristone is an antiprogestogen which competes with progesterone at its receptor. In pregnant women mifepristone's action on the uterus can induce abortion. It causes dilatation of the cervix and increases the sensitivity of the myometrium to the action of prostaglandins. As not all women will abort with mifepristone alone, they are given the prostaglandin misoprostol 36–48 hours after mifepristone.[1]

The recommended dose of mifepristone is a single 200 mg tablet. This is rapidly absorbed. Mifepristone is metabolised by cytochrome P450 3A4, but no interaction studies have been carried out. Some of the metabolites may also act on the progesterone receptor. The final half-life of mifepristone and its metabolites may be up to 90 hours, with most of the dose being excreted in the faeces. Due to a lack of data, mifepristone is not recommended for women with renal failure or hepatic impairment. As the drug has some action on glucocorticoid receptors, adrenal failure is a contraindication. Patients taking corticosteroids, including inhaled corticosteroids, may need to increase their dose.

As mifepristone was first developed in the 1980s, it has been studied in several different regimens and in different stages of pregnancy. A systematic review of medical methods of abortion in the first trimester found that, in combination with a prostaglandin, the 200 mg dose of mifepristone was as effective as a 600 mg dose.[2] In one trial 89.3% of 792 pregnant women, with a menstrual delay of 35 days or less, had a complete abortion after taking mifepristone 200 mg followed by oral misoprostol. The median time to abortion was 51 hours after taking mifepristone.[3]

Beyond the first trimester, mifepristone can be used to prepare for termination of pregnancy, for medical reasons, with prostaglandins. A systematic review of medical methods of second trimester abortion concluded that mifepristone with misoprostol had the highest efficacy.[4] As the efficacy of the combination declines with gestational age[3], up to 30% of women may still need surgical evacuation when the drugs are used after the first trimester.

Although mifepristone has only recently been registered in Australia, it has been used for early medical abortion. An observational study involving 13 345 women used a regimen of oral mifepristone 200 mg followed 24–48 hours later by buccal misoprostol 800 microgram (gestational age ≤63 days). The method only failed in 3.5% of patients, with 2.9% needing surgical evacuation and 0.6% continuing the pregnancy.[5]

The combination of mifepristone and misoprostol commonly causes nausea, vomiting and diarrhoea. Vaginal bleeding is to be expected, but this can be prolonged. In the Australian study the incidence of haemorrhage requiring transfusion was approximately 0.1%.[5] The method is not recommended in women with anaemia. Infection is another potential complication of abortion and one woman died in the Australian study.[5] It is therefore important that women are advised what symptoms to expect and that they are followed up to ensure the abortion is complete and uncomplicated. If the method fails and the woman decides to continue with the pregnancy there is uncertainty about the effects of the drugs on the surviving fetus.

Ectopic pregnancy is a contraindication to mifepristone. If the woman has become pregnant despite having an intrauterine contraceptive device, the device should be removed before mifepristone is used.

In the Australian study most of the women reported medium or heavy bleeding and moderate or severe pain. However, 78% said they would choose the same method again.[5] There is limited evidence comparing medical versus surgical abortion. In a randomised trial involving 122 women who were 13–20 weeks pregnant, pain was rated as moderate to severe by 43% of those who had mifepristone and misoprostol and 23% of those who had surgery. While the women were equally satisfied with their care, only 53% would choose medical abortion again, whereas 100% of the surgical group would choose surgery again.[6]

Although it has taken a long time for mifepristone to be approved in Australia, it has been used in parts of Europe for over 20 years. It adds to the options available when abortion is being considered. While the Australian study showed mifepristone with misoprostol is generally safe for outpatient treatment in early pregnancy, the method will not be suitable for all women. Some will present after the limit of 49 days gestation given in the Australian product information.

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

NEW DRUGS

If mifepristone and misoprostol are used, access to emergency care and follow-up are essential.

T manufacturer provided the product information

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3. Comparison of two doses of mifepristone in combination with misoprostol for early medical abortion: a randomised trial. World Health Organisation Task Force on Post-ovulatory Methods of Fertility Regulation. BJOG 2000;107:524-30.
4. Wildschut H, Both MI, Medema S, Thomee E, Wildhagen MF, Kapp N. Medical methods for mid-trimester termination of pregnancy. Cochrane Database Syst Rev 2011;CD005216.
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6. Kelly T, Suddes J, Howel D, Hewison J, Robson S. Comparing medical versus surgical termination of pregnancy at 13-20 weeks of gestation: a randomised controlled trial. BJOG 2010;117:1512-20.

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The Transparency score (T) is explained in 'New drugs: T-score for transparency', Aust Prescr 2011;34:26–7.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).