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New Applications of Mifepristone (RU 486)

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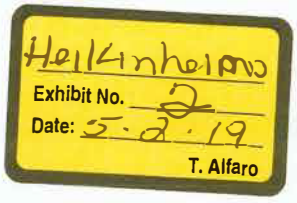

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Mifepristone: Clinical Pharmacology

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Many processes in female reproductive physiology depend on progesterone. This hormone facilitates the action of estradiol in inducing the luteinizing hormone (LH) surge in the follicular phase of the menstrual cycle and supports corpus luteum function in the luteal phase. It is also essential for the initiation and maintenance of pregnancy. A compound that could block the action of progesterone would thus play an important role in the prevention and disruption of pregnancy. With the identification of the progesterone receptor (PR) came the realization that a PR antagonist was a potential candidate for such a compound.

The first highly effective progesterone receptor antagonist was synthesized in 1981 by researchers at Roussel-Uclaf (Romainville, France). Designated RU 38486, and subsequently abbreviated to RU 486, this progesterone antagonist is identified by the generic name mifepristone. In addition to its potent antiprogestin effects, mifepristone also acts as an antiglucocorticoid through its binding to the glucocorticoid receptor. Biologic tests in animals showed that the compound is a potent antagonist for progestins and glucocorticoids.[1]

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Several clinical applications that take advantage of the antiprogestin properties of mifepristone are being pursued.[2] Most well-known are its abortifacient uses. When used alone in early pregnancy, mifepristone causes abortion in 60–80% of women. Its efficacy is enhanced to approximately 95% by the addition of a prostaglandin 48 hours later. Because of its ability to dilate and soften the cervix, mifepristone is used in the preoperative preparation for first trimester surgical abortions as well as pretreatment for prostaglandin-induced first and second trimester abortion. In these applications, it has been shown to decrease pain and side effects, and when used with prostaglandins the interval to expulsion. It is effective for labor induction in late stages of pregnancy in cases of intrauterine fetal death, and its use to induce labor at term is under clinical study.

Another potential use of mifepristone, based on its antiprogestin properties, is as a contraceptive agent. Several different contraceptive methods are undergoing clinical study.[3] Mifepristone has been shown to be highly effective as a post-coital emergency contraception method.[4] Mife-

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