Antiprogestins (Mifepristone and Ulipristal)

These are competitive inhibitors of progestins at progesterone receptors used primarily for termination of pregnancy and emergency contraception.

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Mechanism of Action

Progesterone Receptor Antagonist

Pregnant-Jester with Receptor and Ant-togas

Mifepristone acts as a progesterone receptor antagonist, competitively binding to intracellular progesterone receptors and blocking the effects of progesterone, leading to endometrial breakdown and pregnancy termination. Ulipristal is a selective progesterone receptor modulator that acts as a partial agonist/antagonist, delaying ovulation for emergency contraception.

Indications

Mifepristone

Miffed-priss

Progesterone is fundamental for pregnancy. It is secreted by the corpus luteum until around the tenth week of gestation, after which the syncytiotrophoblast of the placenta produces it for the remainder of pregnancy. Progesterone prepares the endometrium for implantation and maintains pregnancy by preventing endometrial sloughing (menstruation), promoting cervical closure, and inhibiting uterine contractions. Mifepristone antagonizes these effects by blocking progesterone receptors, leading to decidual breakdown, cervical softening and dilation, uterine contractions, and ultimately pregnancy loss.

Pregnancy Termination with Misoprostol

Aborting-Fetus and Miso-frost

Mifepristone, a progesterone receptor antagonist, is used as an abortifacient in combination with prostaglandins such as misoprostol. Medical abortion is performed using oral mifepristone followed by oral misoprostol (a prostaglandin E1 analog, Cytotec). This regimen is approved for use within the first 63 to 70 days of amenorrhea.

Ulipristal

Ulysses-priss

Ulipristal is a selective progesterone receptor modulator (SPRM) used for emergency contraception. It is effective for up to 120 hours (5 days) after unprotected intercourse, although efficacy is highest when taken earlier. Its primary mechanism is delaying or inhibiting ovulation by modulating progesterone receptors, thereby preventing fertilization. It may also cause endometrial changes that could reduce the likelihood of implantation, though this effect is less certain. Ulipristal is considered the most effective oral emergency contraceptive method and requires a prescription in the United States.

Emergency Contraception

Emergency-OCPs

Ulipristal is indicated for preventing pregnancy after unprotected intercourse or suspected contraceptive failure. It is not intended for routine contraception. A single 30 mg oral dose can be taken up to 120 hours (five days) after unprotected sex. Ulipristal works mainly by delaying or inhibiting ovulation. It may also cause endometrial changes that could reduce the likelihood of implantation, although this effect is less certain.

Side effects

Abdominal Pain

Abdominal Pain-Bolt

Cramping or discomfort in the lower abdomen due to uterine contractions, endometrial shedding, or hormonal effects associated with these medications.

Vomiting

Vomit

With mifepristone and ulipristal, vomiting can occur due to hormonal changes affecting the gastrointestinal tract, direct irritation of the stomach lining by the medications, or as part of the systemic response to induced uterine contractions and endometrial shedding. Vomiting may reduce drug absorption and increase the risk of dehydration, requiring monitoring during treatment.

Diarrhea

Toilet

As a side effect of mifepristone and ulipristal, diarrhea may result from hormonal alterations that affect gastrointestinal motility and secretions, or from direct irritation of the gastrointestinal tract by the medications.

Menstrual Irregularities

Irregular Tampon

Both ulipristal and mifepristone can cause menstrual irregularities because both interfere with progesterone signaling, which is crucial for regulating the menstrual cycle.

other mechanisms of action

At High Doses: Cortisol Antagonist

Up-Arrow Ant-toga Court-of-Sol

High doses of mifepristone exert antiglucocorticoid activity by blocking the glucocorticoid receptor. Therefore it has been used at high doses for the treatment of hyperglycemia in patients with Cushing's syndrome, since it blocks the effect of cortisol at the glucocorticoid receptor (antagonizes the effects of cortisol on glucose metabolism) while at the same time increasing circulating cortisol concentrations.

Cushing's Syndrome

Cushion

A glucocorticoid receptor antagonist used to control hypercortisolism in patients with inoperable or refractory Cushing's syndrome.