MECHANISM OF ACTION OF LEVONORGESTREL
EMERGENCY CONTRACEPTIVE PILLS

BACKGROUND

The mechanism of action of emergency contraceptive pills (ECPs) has been a source of confusion since the introduction of ECPs. The FDA-approved label for levonorgestrel ECPs includes a hypothetical mechanism of action suggesting that it may prevent implantation of a fertilized egg in the uterus.¹ A substantial body of evidence indicates that levonorgestrel (LNG) ECPs work primarily – and perhaps exclusively – by delaying or inhibiting ovulation and have no effect once ovulation is imminent.² Based on the evidence the European Medicines Agency removed language suggesting an effect on implantation from the LNG label in 2013,³ yet this language remains on the US labels.

Policy makers and courts in the United States and elsewhere have used this hypothetical mechanism to restrict access to ECPs.⁴ Following the Supreme Court decision in Dobbs v. Jackson Women’s Health Organization (which based on the leaked opinion suggests that it will likely allow states to severely restrict or ban abortion), some state legislatures may look to the language on ECP labels to justify significant restrictions on access to emergency contraception.⁵ This fact sheet describes the scientific research documenting the mechanism of action of LNG ECPs.

QUICK SUMMARY

Levonorgestrel is a progestin (a synthetic form of the naturally occurring hormone progesterone). LNG ECPs work by interfering with the process of ovulation. LNG ECPs impede follicular development and maturation and/or the release of the egg from the ovary.⁶–¹² If there is no egg, fertilization cannot occur. The best available evidence does not support the theory that LNG ECPs can prevent implantation of a fertilized egg.²,¹³

HOW IT WORKS

Pregnancy: For pregnancy to occur, ovulation (release of an egg from the ovary) must occur. Ovulation happens in response to the luteinizing hormone (LH) surge. After ovulation occurs and the egg is released, it must be fertilized by sperm and implanted in the uterine lining. Without implantation of the fertilized egg, pregnancy is not established.

Ovulation: LNG can inhibit the LH surge, impeding follicular development and maturation, and/or ovulation, if taken before the LH surge has begun.⁶–¹²,¹⁴

Implantation: LNG ECPs have not been demonstrated to prevent implantation of a fertilized egg in the uterus.⁶,¹³,¹⁵,¹⁶ Two studies found that 100% of expected pregnancies were prevented by LNG ECPs when taken before ovulation. Those who took LNG ECPs after ovulation got pregnant at the same rate as would be expected if they had not used ECPs at all. Therefore, they are likely ineffective when taken after ovulation and do not prevent implantation of a fertilized egg.¹⁰,¹¹
Sperm: Evidence is mixed about whether LNG ECPs affect sperm function by thickening cervical mucus (thereby inhibiting sperm motility)\textsuperscript{17–20} or interfering with sperm migration.\textsuperscript{10} Other evidence shows that LNG could cause sperm to be hyperactive in the absence of an egg or cause sperm to disorient and move in the wrong direction.\textsuperscript{21–25}

Existing pregnancy: If taken after implantation has occurred, LNG ECPs have no effect on an existing pregnancy and do not increase rates of miscarriage. In the two studies addressing this question, pregnant individuals who had taken LNG EC had the same rates of miscarriage and fetal malformations as those who had not.\textsuperscript{2,26,27,28}

CONCLUSION

The best available evidence indicates that levonorgestrel ECPs prevent or delay ovulation and may inhibit fertilization by interfering with sperm function, but do not prevent implantation. Science supports removing the theoretical mechanism of action about prevention of implantation from FDA-approved LNG ECP labels.
References


