

Metformin

Ovulation Induction

Fact Sheet

Dr Alison Gee - Fertility Specialist
Level 3, 321 Kent Street , Sydney, NSW, 2000.

P (02) 9221 9398 F (02) 9231 3475

Metformin Fact Sheet

What is Metformin?

Metformin is an orally administered medication extensively used in the treatment of type 2 diabetes as an insulin sensitising drug. First reported in 1994, metformin is also prescribed for treating infertility in polycystic ovary syndrome (PCOS) by inducing ovulation (release of eggs).

How does Metformin induce ovulation?

Following a meal, your pancreas releases insulin which allows the organs of your body to uptake glucose (energy) from the food you just ate. When suffering PCOS your body has a decreased sensitivity to insulin for which your body compensates by the pancreas increasing insulin production. The increased levels of insulin acts on the ovaries to increase androgen (male hormones) production which inhibits ovulation.

Metformin is a complex drug which acts upon multiple locations within the body. Ultimately metformin increases your body's sensitivity to insulin which increases glucose uptake by the organs of your body from the bloodstream. This reduction in blood glucose triggers your pancreas to produce less insulin. The reduction in circulating insulin causes your ovaries to produce less androgens and begin ovulating (National Health Service, 2021; Rena et al., 2017).

Why use Metformin to induce ovulation?

While clomiphene citrate (a common ovulation inducing medication) is effective at inducing ovulation in individuals suffering from PCOS, there are others for who it does not. Metformin can be used as an alternative for inducing ovulation in these individuals. Ovulation was 2.5 times more likely, pregnancy was 1.9 times more likely, and live birth was 1.5 times more likely to occur in individuals suffering from PCOS when treated with metformin compared to a placebo or no treatment. In non-obese (a BMI less than 30 kg/m²) individuals, Metformin offers improved rates of pregnancy and live birth compared to clomiphene citrate. However, in obese (a BMI greater than 30 kg/m²) Metformin performs worse than clomiphene citrate with lower pregnancy and live birth rates.

Some individuals suffering from PCOS may not ovulate in response to treatment with either metformin or clomiphene citrate. Treating with both metformin and clomiphene citrate offers increased ovulation and pregnancy rates compared to treatment with only Clomiphene Citrate in those suffering PCOS. In obese PCOS suffers, treating with both metformin and clomiphene citrate improved ovulation and pregnancy rates compared to treating with metformin alone (American Society for Reproductive Medicine, 2016; Costello et al., 2019).

What are some side effects of Metformin?

PCOS suffers receiving metformin for inducing ovulation tolerate it very well. Metformin treatment can cause:

- ✘ Nausea
- ✘ Abdominal bloating
- ✘ Flatulence
- ✘ Vomiting or diarrhoea (in severe cases)

Kidney failure or severe liver disease can increase the risk of a very rare side effect of metformin called lactic acidosis (acidification of the blood), (National Health Service, 2021).

References

- American Society for Reproductive Medicine (2016) Medications for Inducing Ovulation. Available from: https://www.reproductivefacts.org/globalassets/rf/news-and-publications/bookletsfact-sheets/english-fact-sheets-and-info-booklets/booklet_medications_for_inducing_ovulation.pdf.
- Costello, M., Garad, R., Hart, R., Homer, H., Johnson, L., Jordan, C., Mocanu, E., Rombauts, L., Teede, H., Vanky, E., Venetis, C., & Ledger, W. (2019) A Review of First Line Infertility Treatments and Supporting Evidence in Women with Polycystic Ovary Syndrome. *Medical Sciences (Basel)*. 7(9) 95. Available from: <https://dx.doi.org/10.3390%2Fmedsci7090095>.
- National Health Service (2021) Use of Metformin for PCOS. Available from: <https://www.royalberkshire.nhs.uk/patient-information-leaflets/endocrinology-use-of-metformin-in-pcos>.
- Rena, G.; Grahame Hardie, D.; Pearson, E. (2017) The mechanisms of action of metformin. *Diabetologia*. 60(9), 1577-1585. Available from: <https://dx.doi.org/10.1007%2F00125-017-4342-z>.