Use of Metformin in PCOS

Background
Doctors are still not entirely clear why some women develop polycystic ovary syndrome (PCOS). There is often a hereditary link and a link with diabetes in the family. In recent years it has become clear that PCOS is closely related to a problem with insulin. Insulin is a hormone released from the pancreas after a meal and it allows the organs of the body to take up energy in the form of glucose. In PCOS there is a 'resistance' of cells in the body to insulin, so the pancreas makes more insulin to try and compensate. The excessively high levels of insulin have an effect on the ovary, causing a rise in androgen (testosterone) levels and preventing ovulation. It may also make weight loss more difficult.

Reducing insulin levels by weight loss, exercise or drugs results in a lowering of testosterone and an improvement of the symptoms of PCOS. Metformin is a drug which has been used in the treatment of diabetes for over 30 years. It acts by making the body more sensitive to insulin. Since it does not stimulate production of insulin, it does not cause low blood glucose levels.

The use of Metformin in women with PCOS
There have been several studies looking at the use of Metformin in women with PCOS and the majority have shown that Metformin can make periods more regular and improve fertility in women with PCOS. The use of Metformin may also make weight loss easier. Finally, it may also help reduce hirsutism although this may take several months and Metformin may not be as effective as other treatments for hirsutism. If unwanted hair growth is a concern in women not seeking pregnancy, another drug called Spironolactone is added to the treatment.

Metformin works best in overweight women with PCOS. However, it is less effective in women who are markedly obese. Its effects are enhanced by weight loss.

All the evidence is that Metformin is safe in pregnancy and recent studies have shown that taking it up to 12 weeks of pregnancy may reduce the risk of miscarriages.

Side effects
Metformin can cause nausea, abdominal bloating and flatulence. In severe cases, it can cause vomiting or diarrhoea. Most women tolerate it very well, particularly if the dose is increased gradually. Additionally, to minimise side effects, the tablets should be taken in the middle of a meal or straight after a meal. Side effects usually settle after 1-2 weeks.
Women with kidney failure or severe liver disease should not take Metformin. As patients with kidney damage or significant liver disease are at an increased risk of a very rare side effect of Metformin called lactic acidosis, we always check your kidney and liver functions before prescribing this drug for you.

Metformin has been used in the treatment of diabetes for over 30 years and has not been associated with any other side effects. However, Metformin is only licensed for the treatment of diabetes, not PCOS. Metformin is not an experimental drug but its use in PCOS is relatively new.

**Starting Metformin in PCOS**

Quick route:
500mg a day for 1 - 2 weeks then
500mg twice a day for 1 - 2 weeks then
500mg three times a day or 850mg twice a day for 1 - 2 weeks then
1g twice a day or 850mg three times a day thereafter

Do not increase the dose if side effects develop - wait until they have settled first.

Slow route (in women with side effects):
Week 1  250mg once a day
Week 2  250mg twice a day
Week 3  250mg three times a day
Week 4  500mg twice a day
Week 5  500mg three times a day
Week 6  1g twice a day

There is no particular time limit for the use of Metformin. However if after six months of use no beneficial effect has been seen then discontinuing the drug could be considered.

More information is available on the Trust website [www.royalberkshire.nhs.uk](http://www.royalberkshire.nhs.uk)

This document can be made available in other languages and formats upon request.

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