

Metformin for treating polycystic ovary syndrome in women who are not trying to get pregnant

Information for the public

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About this information

This information explains the evidence summary about the off-label use of metformin for polycystic ovary syndrome in women who are **not** trying to get pregnant. It does not cover metformin use in women who are trying to get pregnant. The evidence summary is an overview of the available information about this medicine. It aims to help prescribers and patients when they are considering whether or not to use an unlicensed or off-label treatment. The summary does not contain recommendations from NICE on whether the medicine should be used.

Licensing medicines

In the UK, medicines need to have a licence before they can be marketed. To get a licence, the manufacturer of the medicine has to provide evidence that shows that the medicine works well enough and is safe enough to be used for a specific condition and for a specific group of patients, and that they can manufacture the medicine to the required quality. Medicines can be prescribed without a licence (an 'unlicensed medicine') if there is no suitable licensed alternative and it is likely to benefit the patient.

A medicine can also be prescribed 'off-label'. This means the medicine has obtained a license but the prescriber wants to use it in a different way than is set out in the terms of its licence. This could mean using the medicine for a different condition or a different group of patients, or it could mean a

change in the dose or that the medicine is taken in a different way. There is more information about licensing medicines on [NHS Choices](#).

What is polycystic ovary syndrome?

Polycystic ovary syndrome (or PCOS for short) is a condition that affects how a woman's ovaries work. To understand how metformin might help in PCOS, it is necessary to understand a little about the role some hormones play in the condition.

Many, but not all, women with PCOS also have what is known as 'insulin resistance'. This is when the cells in their body do not respond as well as normal to insulin (the hormone the body produces that controls blood sugar levels). Insulin resistance in turn leads to a person having levels of insulin in their body that are higher than normal. These high levels of insulin can cause the normal balance of male and female hormones to be disturbed. More male hormones are produced leading to some of the symptoms of PCOS, such as excessive body hair (known as hirsutism), acne, period problems and problems getting pregnant. Higher levels of insulin can also cause people to gain weight; many women with PCOS are overweight or obese. These hormonal changes also mean that women with PCOS have a higher risk of developing type 2 diabetes (especially if they are also obese) and endometrial cancer (cancer in the lining of the womb).

For women with PCOS who are not trying to get pregnant, a drug called co-cyprindiol is licensed in the UK to treat severe acne that has not improved after the long-term use of oral antibiotics and excessive hair growth (although not specifically in PCOS). Brand names for co-cyprindiol include Acnocrin, Cicaferm, Clairette and Dianette. Co-cyprindiol contains a drug called cyproterone, which blocks the effects of male hormones on the skin. Co-cyprindiol also acts as an oral contraceptive and regulates a woman's menstrual periods. Oral contraceptive pills, which don't contain cyproterone, can also be used to regulate periods, but this use is 'off-label' (see [licensing medicines](#) for more information). Other treatment options, such as losing weight, and other treatments for acne, may be appropriate for individual women and they should discuss these with their doctor.

There is more information about polycystic ovary syndrome on [NHS Choices](#).

About metformin

Metformin is a drug commonly used for controlling blood sugar levels in people with diabetes. It helps improve the ability of cells in the body to respond to the normal actions of insulin. Many women with PCOS have what is known as 'insulin resistance' (see '[what is polycystic ovary disease?](#)'). The effects of metformin on the body's response to insulin suggest it might be helpful in

managing the symptoms of PCOS, for example in women who don't want to take other treatments or for whom these aren't suitable.

Metformin has a license in the UK for treating type 2 diabetes, particularly for people who are overweight. However it does not have a license for use in PCOS, so use in this way is described as 'off-label'.

It is important to note that metformin is not a contraceptive. Sometimes, women with PCOS who have not got pregnant before taking metformin have got pregnant after starting to take it. In fact, NICE recommends metformin as a treatment option in certain circumstances for women with PCOS who want help to get pregnant. Women with PCOS who do not want to get pregnant but who are thinking about taking metformin to control some of the symptoms of PCOS should discuss their contraceptive needs and options with an appropriate health professional.

Summary of possible benefits and harms

How well does metformin work?

Seven small studies have looked at how well metformin, used on its own, worked compared with co-cyprindiol. Overall, these studies could not reliably say if metformin was better or worse than co-cyprindiol in improving excessive hair growth and acne. Metformin did not work as well as co-cyprindiol at regulating periods in 2 studies. Four other studies could not reliably say if metformin was better or worse than co-cyprindiol in regulating periods.

Two small studies looked at the combination of metformin and co-cyprindiol compared with co-cyprindiol or metformin used on their own. These studies could not reliably say if there was a difference between these treatments in improving excessive hair growth or regulating periods.

All these studies had only small numbers of women and so these findings may not be accurate. Two other studies looked at metformin compared with oral contraceptives but they did not have enough women to draw reliable conclusions.

The length of treatment in the studies was up to 6 months, so it isn't known how well metformin may work over longer periods. It is also not possible to say from these studies if metformin has any effect in the longer term on the development of diabetes or endometrial cancer.

What are the possible harms or side effects?

Metformin is most often used in people with diabetes. Based on that experience, the most common side effects are problems affecting the stomach and bowel, such as feeling sick (nausea), being sick (vomiting), diarrhoea, stomach (abdominal) pain and loss of appetite. These side effects occur in more than 1 in 10 people taking metformin but they most often happen at the beginning of treatment. Spreading the doses over the day and taking the tablets with or straight after a meal can help reduce these side effects.

Based on the evidence available, more women with PCOS taking metformin had side effects affecting the stomach and bowel than women taking co-cyprindiol. However, co-cyprindiol was more likely than metformin to cause other side effects such as weight gain, high blood pressure, depression, chest pain and headache. The studies comparing metformin and co-cyprindiol had only small numbers of people so these findings may not be accurate.

Prescribing metformin

If a prescriber wants to use an unlicensed or off-label medicine, they must follow their professional guide, for example for doctors the General Medical Council's [good practice guidelines](#). These include giving information about the treatment and discussing the possible benefits and harms so that the patient has enough information to decide whether or not to have the treatment. This is called giving informed consent.

The full version of the summary aimed at healthcare professionals is available at <http://publications.nice.org.uk/esuom6-polycystic-ovary-syndrome-metformin-in-women-not-planning-pregnancy-esuom6>. The summary for healthcare professionals does not contain recommendations from NICE on whether the medicine should be used.

If your doctor is suggesting that you might try metformin for PCOS, you might like to ask some of the questions below.

Questions to ask

- Why am I being offered an off-label medicine?
- What does the treatment involve?
- What are the benefits I might get?

- How good are my chances of getting those benefits?
- Could having the treatment make me feel worse?
- Are there alternative treatments?
- What are the risks of the treatment?
- Are the risks minor or serious? How likely are they to happen?
- What may happen if I don't have the treatment?

More information

The evidence summary and this information for the public were produced for NICE by Bazian Ltd.

NICE has published [information](#) about how evidence summaries for unlicensed and off-label medicines are developed.

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