

# Specialists In Reproductive Medicine & Surgery, P.A.

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## Metformin Hydrochloride Patient Information

### Indications:

Metformin is indicated, in addition to weight reduction and a sensible diet, to lower blood glucose levels in patients with Type II Non-Insulin-Dependent Diabetes Mellitus (NIDDM).

While not FDA approved, Metformin may help patients with Polycystic Ovarian Syndrome (PCOS), reduce elevated insulin levels (insulin resistance) and decrease glucose levels (glucose intolerance). The excess insulin stimulates the ovary to produce male hormones, which in turn, results in some of the PCOS signs and symptoms. *Insulin resistance with or without glucose intolerance should be considered prediabetes.* Metformin may also be used for male-factor infertility patients.

### Anatomy/Physiology/Mode of Action:

Patients with insulin resistance are unable to fully utilize the insulin their body produces in combination with the glucose they consume. Without treatment, the elevated insulin and glucose levels can result in hypertension, heart disease, abnormal uterine bleeding, abnormal hair growth, acne, uterine cancer and infertility. Metformin seems to work through several mechanisms:

1. It reduces glucose production from the liver which reduces both glucose and insulin levels (primary mode of action).
2. Decreases the intestinal absorption of glucose.
3. Metformin reduces glucose levels in Type II diabetics but has no effect on glucose levels in nondiabetic patients.
4. Improves insulin sensitivity helping to move the glucose in your bloodstream into the cells.
5. Decreases total cholesterol, triglycerides and LDL while leaving the “good” cholesterol levels essentially unchanged or even slightly improved.
6. Metformin decreases male hormone levels in women.
7. Decreases high blood pressure (hypertension).
8. Induces moderate weight loss which, in and of itself, may increase the potential for spontaneous ovulation and pregnancy.
9. Metformin increases the effectiveness of ovulation medications making it more likely for a patient to ovulate and potentially conceive.
10. Metformin may delay the onset of diabetes. True prevention of diabetes will generally only occur in combination with diet, exercise and (substantial) weight loss.
11. Some studies suggest that Metformin will reduce pregnancy loss rates, which is why the medication may be provided to all PCOS patients regardless of presence or absence of prediabetes.
12. There is no data to suggest that Metformin increases the risk of a *multiple* pregnancy.

13. In men with prediabetes or diabetes, Metformin increases testosterone levels as well as improving semen parameters including concentration, motility and normal forms.

### **Contraindications To Taking The Medications:**

#### **Absolute Contraindications:**

- Metformin is to be given carefully in patients with known kidney or heart disease.
- Metformin should not be given to patients with an allergy to the drug.

#### **Relative Contraindications:**

- Alcohol should be minimized while taking this drug.

### **Adverse Drug Effects:**

1. About 30% of the patients will experience some level of diarrhea, nausea, vomiting, abdominal bloating, gas or loss of appetite when first starting the medication. The symptoms generally resolve within a couple of weeks with only 4% of the patients having to stop the medication because of intestinal upset. ***Significantly reducing your carbohydrate intake commonly reduces the onset and severity of these symptoms. Carbohydrates should be reduced prior to starting as well as when taking this medication.***
2. If you are to undergo a hysterosalpingogram (HSG), please do not take Metformin during the day prior, the day of, and the two days following the HSG (total of four days). This same precaution should be used if any other studies with iodinated contrast materials including major surgery.
3. Because the medication is excreted through the kidneys, it is important to stay well hydrated in the hot Florida sun to keep levels of the drug from building up.
4. There is a rare complication that can occur called lactic acidosis. This complication is seen in only 1 out of 33,000 patients who take the drug for one year. This severe complication generally occurs in older patients that are truly diabetic and often suffering from kidney disease. The symptoms include extreme weakness, feeling tired or uncomfortable, unusual muscle pain, trouble breathing, unusual or unexpected stomach discomfort, feeling cold, dizzy or lightheaded and a slow or irregular heartbeat. One should have several the above symptoms before being concerned with lactic acidosis. Realistically, the chances of developing lactic acidosis may be almost non-existent in the patient population here at **SRMS**.

### **Drug Interactions:**

1. The interaction with other medications is minimal.
2. Metformin seems to be slightly better tolerated when taken with food. It may also be best for the female patient to take a prenatal or multivitamin each day while taking this medication.

### **Pregnancy:**

Metformin has not been found to produce abnormalities in newborn humans, rats or rabbits (Class B). The placenta seems to form a partial barrier to the drug. Your physician may feel that it is best that you take this medication during early pregnancy. Metformin may reduce sugar levels for some patients which are associated with fetal malformations. Continuing the medication during pregnancy seems to reduce the incidence of gestational diabetes. It will be up to your delivering Obstetrician to decide if it will be continued throughout your pregnancy. Breast feeding concerns will need to be discussed with your Pediatrician.

### **Where Can I Find Out More About The Drug?**

Package insert and the following sites on the WEB:

<https://www.ncbi.nlm.nih.gov/pubmed/> (type in “metformin and polycystic ovarian disease”)

### **Dosage & Administration:**

Because intestinal disturbances are seen in one-third of the patients, it is suggested that you take the medications in the following manner and don't forget to reduce your carbohydrate intake:

Week 1: 500 mg., one pill with the morning meal (1 pill/day)

Week 2: 500 mg., one pill twice each day with morning and evening meals (2 pills/day)

Week 3: 500 mg., one pill three times each day with meals (3 pills/day)

If you are requested to take multiple doses of Metformin each day and are unable to do so because of intestinal side effects, reduce the number of pills consumed each day for one week while you further reduce your carbohydrate intake. After reducing the number of pills you take each day for one week, please try to increase your dose back to the recommended amount.

Extended release formulations may also reduce the side effects of Metformin but are generally more expensive. They do allow, for example, the patient to take larger dosages of the medication (850 – 1000 mg) less frequently throughout the day. If necessary, your clinician may need to increase your dose up to 850 mg three times each day.

***Please do not discontinue Metformin without consultation with your clinician.***

### **Alternative Medications:**

There are alternatives to Metformin that have fewer side effects but these are commonly more expensive, require occasional blood testing and far less studied in the reproductive age patient. If you are unable to tolerate Metformin, please contact SRMS and we will consider prescribing an alternative medication.

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