



830 Oak Street
Brockton, MA 02301
(508) 583-4961
Fax (508) 583-4732
Soheil.Hanjani@Steward.org

METFORMIN

What Is Metformin?

Metformin (Glucophage) is a drug (an oral biguanide antihyperglycemic agent) approved for the treatment of adult-onset (type 2) diabetes mellitus. It is used to help control blood glucose levels in people. It has been used in Europe for over 25 years, and in the US since 1995. The FDA has approved Metformin only for the treatment of Type 2 Diabetes. Metformin is also used to treat Polycystic ovary disease (PCOD), although this indication is not approved by the U.S. Food and Drug Administration (FDA). It is also used in infertility treatment, again a non-FDA approved indication.

Metformin appears to work in three ways. First, it decreases the absorption of dietary carbohydrates through the intestines. Second, it reduces the production of glucose by the liver. The liver uses the raw material in your food to create a reserve supply of blood sugar. When your body experiences stress, the liver releases the reserve glucose to supply your brain and muscles with an immediate source of energy to cope with the stress. Metformin suppresses the production of this reserve fuel. Third, and perhaps most importantly, Metformin increases the sensitivity of muscle cells to insulin. Insulin is the hormone that delivers glucose into your cells to be burned as fuel, or stored. Women with Polycystic ovary syndrome (PCOS) frequently have "insulin resistance", a condition where excessive amounts of insulin are required in order to get blood glucose moved into cells, where it belongs. Metformin helps your body to transport glucose with relatively less insulin, thus lowering your insulin levels. Chronically high levels of either glucose or insulin in your blood contributes to obesity, heart disease, infertility, and certain cancers, as well as the development of diabetes.

Benefits of Metformin

LOWERING OF INSULIN, TESTOSTERONE, AND GLUCOSE LEVELS. Quite a number of studies indicate Metformin reduces insulin, testosterone and glucose levels -- which reduces acne, hirsute, abdominal obesity, amenorrhea and other symptoms.

PREVENTION OR DELAY OF ONSET OF DIABETES AND REDUCED RISK OF GESTATIONAL DIABETES. Metformin may help to prevent diabetes and reduce the risk of developing gestational diabetes in PCOS patients.

RESTORATION OF NORMAL MENSTRUAL CYCLE. Metformin can help restore menstruation to normal in many women with PCOS.

IMPROVED CHANCE OF PREGNANCY. As well as helping regulate menstrual periods, Metformin helps induce ovulation at times. To achieve pregnancy though fertility medication, such as clomiphene may also be required.

REDUCED RISK OF MISCARRIAGE. Another aspect of PCOS-related infertility is the tendency for repeated miscarriages. Metformin may reduce the miscarriage rate in PCOS patients.

WEIGHT LOSS AND OTHER BENEFITS. Metformin may contribute to weight loss in some diabetics. However, weight loss does not appear to be one of its primary benefits. Metformin may also be of some value improving success with in vitro fertilization, lowering cholesterol, and improving energy.

Side Effects of Metformin

MALAISE. 10%- 25% of women who take Metformin just don't feel well. They experience a general malaise, fatigue and occasional achiness that lasts for varying lengths of time. If you develop malaise you will need liver, kidneys, and GI tract tests. A blood count should be taken from time to time, because Metformin can induce B vitamin insufficiencies that can lead to a form of anemia.

GI DISTURBANCE. About one third of women on Metformin experience gastrointestinal disturbances, including nausea, occasional vomiting and loose, more frequent bowel movements, or diarrhea. This problem occurs more often after meals rich in fats or sugars. The symptoms lessen over time, so if you can tolerate the GI upset for a few weeks, it may go away. One "benefit" of these unpleasant symptoms is that you find yourself eating less and thus losing some weight.

VITAMIN B12 MALABSORPTION. Of patients who take this drug, 10%-30% show evidence of reduced vitamin B12 absorption. Over the long term, vitamin B12 insufficiency can be a significant health risk. At least one study raises the concern that even if Metformin is withdrawn, the vitamin B12 malabsorption may continue in some people

ELEVATED HOMOCYSTEINE. People who take Metformin tend to have higher homocysteine levels. Women with PCOS also tend to have elevated homocysteine. Homocysteine is an amino acid in the blood and elevated levels means that your metabolic processes are not working properly. Elevated homocysteine is associated with coronary artery disease, heart attack, chronic fatigue, fibromyalgia, and higher risk of cervical cancer.

ELEVATED HOMOCYSTEINE & PREGNANCY COMPLICATIONS. Pre-eclampsia is a complication of pregnancy characterized by increasing blood pressure and edema. Elevated homocysteine, not Metformin itself, could contribute to pregnancy complications in some women. However, Metformin does contribute to increased homocysteine levels.

PREGNANCY WARNING. Many women use Metformin in their pursuit of a successful pregnancy. However, Metformin is a category B drug, meaning its safety for use while pregnant has not been fully established, but it is thought to be relatively safe. It is found in breast milk so it's not advisable to breast feed while taking Metformin.

ANEMIA. By preventing optimal absorption of vitamins B12 and folic acid, Metformin could induce or contribute to megaloblastic anemia. Although anemia is not common among people taking Metformin, it remains a risk for those whose B12 and folic acid levels were already low when Metformin therapy was started.

LIVER OR KIDNEY PROBLEMS. If you have liver or kidney problems of any kind, Metformin could pose a problem, because it alters liver function and is excreted through the kidneys. A healthy liver and kidneys will improve your outcome with Metformin. Liver and kidney function should be assessed before starting Metformin and rechecked at least once a year while taking it.

MULTIPLE MEDICATIONS. You may be at risk for health problems or symptoms if you take Metformin in addition to other medications. The more drugs you take, and the higher the dosage, the greater the probability there will be some kind of interaction between the drugs or some unexpected effect from the combined drugs. The effect of combined drugs also depends on the state of your health, your genetic uniqueness, and your diet and lifestyle.

HAIR LOSS. There is a small possibility that Metformin may contribute to hair loss.

LACTIC ACIDOSIS. About 3 of every 100,000 people who take Metformin will develop a medical emergency called "lactic acidosis". Lactic acid is a metabolic byproduct that can become toxic if it builds up too fast. Lactic acidosis is most likely to occur in people who with diabetes, kidney or liver disease, multiple medications, dehydration, or severe chronic stress. Lactic acidosis can gradually build up. Symptoms to watch for include a need to breathe deeply and more rapidly, a slow, irregular pulse, a feeling of weakness, muscle pain, sleepiness, and a sense of feeling very sick. Treatment requires intravenous administration of sodium bicarbonate. Contact me or go immediately to a hospital emergency room if you have these symptoms.

What to Do if You Are Taking Metformin

IMPROVE YOUR DIET AND INCREASE EXERCISE. If you improve your diet and increase your level of exercise, you may be able to reduce or eventually eliminate your Metformin therapy. There's no question that healthy diet, exercise and lifestyle habits will significantly improve PCOS-related health problems, as well as reduce the risk of diabetes and cardiovascular disease.

CONSIDER SPECIAL NUTRIENT THERAPY. You should protect yourself by taking a B-complex vitamin and a multiple vitamin & mineral supplement as well as extra calcium, magnesium and Vitamin D.

AVOID DEHYDRATION AND ALCOHOL. It is very important to avoid getting dehydrated or drinking alcohol to excess alcohol when on metformin as these will increase the risk of side effects significantly and can be dangerous.

Blood tests – you will need blood tests before starting Metformin, especially kidney function tests.

Dosage

Dosage: 1,500 mg per day, in divided doses of 500mg three times a day with meals. To reduce the chance of side effects you will be started on a low dosage and the dose will be increased incrementally.

If needed the dosage can be changed to delayed release metformin, Metformin XR 850mg once a day.

When used for infertility, Metformin is usually started and 1-2 months later clomiphene (clomid) or Letrozole (Femara) is used to help induce ovulation.