

**OVERVIEW**

Metformin is a biguanide antihyperglycemic agent which lowers glucose levels in diabetics by decreasing insulin resistance. (See Mechanisms of Action & Advantages. It has been approved for general outpatient use by the University Health System Faculty & Housestaff.

**INDICATIONS**

Metformin is indicated for Type II (NIDDM) patients who have failed adequate control on diet (monotherapy) or as concomitant therapy with a sulfonylurea or insulin to improve glycemic control.

**CONTRAINDICATIONS**

Nearly all reported cases of potentially fatal lactic acidosis have been reported in patients in whom use of metformin was contraindicated.

- **Renal Insufficiency:** Assess renal function before initiation of therapy (and at least annually). Do not use if serum creatinine 1.5 mg/dL in males, 1.4 mg/dL in females, or if creatinine clearance is <70 mL/minute.
- **Liver Disease:** Assess liver function before initiation of therapy. Patients with LFTs >2.5 times normal are not candidates since the liver is the primary organ of lactic acid homeostasis. Alcohol may be hepatotoxic when ingested in large quantities, therefore, the patient should be warned about "binge drinking" (>2 drinks/day).
- **Acute Cardiopulmonary Disease:** Pulmonary disease, CHF requiring pharmacologic treatment, or conditions associated with tissue hypoxia (trauma, dehydration, severe infection).
- **Pregnancy, Lactation, and Pediatric:** Safety has not been established.
- **Hospitalization:** Therapy should be temporarily suspended for surgical procedures, radiologic procedures involving contrast dyes, or loss of glycemic control due to fever, trauma, or infection. Thus, metformin has been restricted to outpatient use only. In outpatients undergoing radiological studies involving the use of contrast dyes, metformin should be discontinued at the time of or prior to the procedure, and withheld for 48 hours or until renal function has been re-evaluated.

**MECHANISMS OF ACTION AND ADVANTAGES**

- Does not stimulate the release of insulin
- Decreases hepatic glucose production
- Increases insulin sensitivity by increasing glucose uptake by the muscle
- Associated with modest weight loss
- Exhibits favorable effects on the lipid profile

**DOSING AND AVAILABILITY**

Metformin is available in 500 mg and 850 mg tablets. The maximum daily dosage is 2500 mg (5 of the 500 mg tablets) or 2550 mg (3 of the 850 mg tablets). The tablets should be taken with meals to minimize GI side effects (anorexia with or without vomiting, diarrhea, and bloating). Slow titration as shown in table below will also minimize early intolerance due to GI side effects.

TIME*	WEEK 1	WEEK 2	WEEK 3
Breakfast	500 mg	1000 mg	1000 mg
Lunch			
Supper	500 mg	500 mg	1000 mg

**\*It may be preferable to take twice daily doses with the two largest meals of the day.**

**ADDITIONAL PRECAUTIONS**

In addition to the specific contraindications listed, other precautions are necessary to avoid adverse effects.

- Read the full prescribing information of the package insert, especially the boxed warning regarding lactic acidosis.
- Patients should be advised to read the available patient information leaflet and notify their physician promptly if they have unexplained difficulty breathing, muscle cramps, nausea with vomiting, or dehydration.
- Use caution in the elderly; titrate dose slowly; they should not be titrated to the maximum dose.

**MONITORING AND DOCUMENTATION**

In addition to renal function and liver function, hematologic parameters, fasting plasma glucose, and glycosylated hemoglobin should be used to determine effects and therapeutic response.

**Goals of therapy and patient counseling information should be clearly documented in the chart.**