

## Name(s)

- **Generic:** metformin (*met FOR min*) | **Brand:** Glucophage, Glucophage XR, Glumetza, Riomet, Riomet ER

## Therapeutic Category

- Biguanide | Anti-Diabetic Agent

## Indication(s)

1. **Type 2 Diabetes mellitus (T2DM):** If tolerated and not contraindicated, it is the preferred pharmacologic agent when hyperglycemia cannot be managed through diet and exercise.
- **OFF LABEL (Not explored, exception \*GDM):** Antipsychotic-induced weight gain; Prevention of T2DM; **Gestational diabetes mellitus (GDM);** Polycystic ovary syndrome (PCOS), Oligomenorrhea due to PCOS, Ovarian hyper-stimulation syndrome (OHSS) in women w/ PCOS undergoing in vitro fertilization

## Dosage Form / Strength / Dosing

- **Dosage Form:** Immediate Release (IR) Tablet, Extended Release (ER) Tablet, Solution/Suspension (ER)
  - IR Tablets: 500 mg, 750 mg, 850 mg, 1000 mg
  - ER Tablets: 500 mg, 750 mg
  - Solution/Suspension: 500 mg/5 ml (IR, ER) (Rarely used/covered by insurance so not discussed further)
- Dosing Contraindications:
  - Severe renal dysfunction (eGFR <30 mL/min/1.73 m<sup>2</sup>)
  - Metabolic acidosis w/ or w/o coma (acute, chronic, ketoacidosis)
- **Dosing for Type 2 Diabetes mellitus (T2DM):** **Adult** & Geriatric (but conservative dosing w/ geriatric)
  - When not reaching glycemic targets through diet and exercise
  - IR Tablets
    - Start with 500 mg 1-2 times daily OR 850 mg once daily.
    - Gradually increase to minimize GI issues. Titrate by 500 mg to 850 mg increments every 7 days.
    - Maintenance dose is 850 mg to 1000 mg twice daily
    - Max: 2.55 g/day. If >3 g/day is needed consider dividing dosing to three times a day dosing.
  - ER Tablets (NOTE: Less GI issues from ER formulations)
    - Start with 500 mg to 1000 mg once daily, gradually dose adjust to 2000 mg once daily
    - Max: 2 g/day. May divide dose to twice daily for additional control if not achieved at once daily.
- **Dosing for Type 2 Diabetes mellitus (T2DM):** **Pediatrics** (≥ 10 years and Adolescent)
  - IR Tablets
    - Start with 500 mg to 1000 mg 1-2 times daily.
    - Gradually every 1-2 weeks to minimize GI issues titrating in 500 mg to 1000 mg increments.
    - Maintenance dose is 850 mg to 1000 mg twice daily; Max: 2 g/day
- (OFF LABEL) **Dosing for Gestational diabetes mellitus (GDM)**
  - IR Tablets:
    - Start with 500 mg 1-2 times daily w/ gradually titrated doses every 1-2 weeks with max dose of 2 – 2.5 g/day divided into 2-3 doses/day.



- Important to note that **insulin** is the **preferred agent** because it does not cross the placenta and oral **metformin lacks long-term safety data**.

## Mechanism of Action & Pharmacology

- Hepatic glucose production and intestinal glucose absorption is decreased. Peripheral glucose uptake and utilization is increased which increases insulin sensitivity.
- **Metabolism:** Not metabolized by the liver, 90% excreted in urine (so renal considerations when dosing)
- **Onset of Action:** max effects up to 2 weeks; **Time to Peak:** IR 2-3 hours; ER 4-8 hours; ER Suspension 3.5-6.5 hours; **Half-Life:** 4-9 hours (plasma) and 17.6 hours (blood); Not protein bound

## Side Effects

- More commonly (>10%): **Diarrhea, flatulence**, nausea, vomiting, **infection**
- Others (1-5%, 7%, or <10%): Chest discomfort, flushing, diaphoresis, chills, upper respiratory infections, rhinitis, flu-like symptoms

**BLACK BOX WARNING:** **Lactic acidosis** - Can result in death, hypothermia, hypotension, and bradyarrhythmias. Onset is subtle w/ symptoms such as malaise, myalgias, respiratory distress, and abdominal pain. Look for elevated blood lactate levels > 5mmol/L, anion gap acidosis, metformin plasma levels > 5 mcg/mL. **Risk factors** are renal impairment, recent iodinated contrast dye agent usage, use of drugs like carbonic anhydrase inhibitors (topiramate), ≥65 years, hypoxic states (acute CHF), excessive alcohol intake, hepatic impairment

## Drug Interactions

- Increases toxic effects: alcohol (ethyl), carbonic anhydrase inhibitors (topiramate), iodinated contrast dyes, NSAIDs, various antivirals (ombitasvir, paritaprevir, ritonavir)
- Increases serum concentrations: cephalexin, cimetidine, dolutegravir, glycopyrrolate, lamotrigine
- Others: Quinolones, salicylates, SSRIs

## Monitoring Parameters

- Urine (glucose, ketones), Blood glucose (fasting), HbA<sub>1c</sub> (≥Twice/year), renal function tests

## Patient Counseling Information

- Used to lower blood sugar; Take with meal to decrease GI upset (gas, diarrhea, nausea, vomiting)
- Identify **low blood sugar signs** as dizziness, headache, fatigue, weakness, **sweating**
- **Pregnancy:** Crosses placenta, adverse fetal/neonatal outcomes not observed, Glycemic control should be achieved prior to pregnancy.

## Reference(s)

- <https://www.drugs.com/ppa/metformin.html>

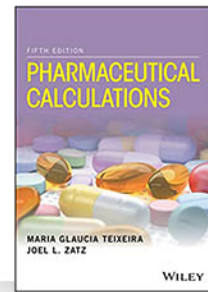
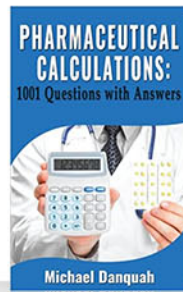


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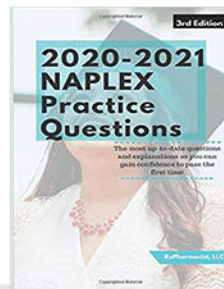
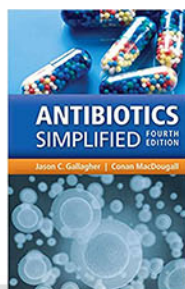
## Calculations (NAPLEX)



## Pharmacy Law (MPJE)



## Supplemental



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