

# [Metformin (glucophage) reactions](https://assignbuster.com/metformin-glucophage-reactions/)

Metformin (Glucophage) is available in the Pakistan since 1998. It falls in the same drug class as phenformin. Metformin is considered a first line agent and is significantly useful in people with known insulin resistance

GLUCOPHAGE® (metformin hydrochloride tablets) and GLUCOPHAGE® XR (metformin hydrochloride extended-release tablets) are oral antihyperglycemic drugs used in the management of type 2 diabetes. Metformin hydrochloride (N, N-dimethylimidodicarbonimidic diamide hydrochloride) is not chemically or pharmacologically related to any other classes of oral antihyperglycemic agents. The structural formula is as shown:

### Glucophage (metformin hydrochloride tablets) Structural Formula Illustration

Metformin hydrochloride is a white to off-white crystalline compound with a molecular formula of C4H11N5 • HCl and a molecular weight of 165. 63.

Metformin improves hyperglycemia primarily through its suppression of hepatic glucose production, especially hepatic gluconeogenesis[1]. The “ average” person with type 2 diabetes has three times the normal rate of gluconeogenesis; metformin treatment reduces this by over one third.[2] Metformin activates AMP-activated protein kinase (AMPK), a liver enzyme that plays an important role in insulin signaling, whole body energy balance, and the metabolism of glucose and fats;[3] activation of AMPK is required for metformin’s inhibitory effect on the production of glucose by liver cells.[4] Research published in 2008 further elucidated metformin’s mechanism of action, showing that activation of AMPK is required for an increase in the expression of SHP (Small heterodimer partner), which in turn inhibits the expression of the hepatic gluconeogenic genes PEPCK and Glc-6-Pase.[5] Metformin is frequently used in research along with AICAR as an AMPK agonist. The mechanism by which biguanides increase the activity of AMPK remains uncertain; however, research suggests that metformin increases the amount of cytosolic AMP (as opposed to a change in total AMP or total AMP/ATP).[6]

In addition to suppressing hepatic glucose production, metformin increases insulin sensitivity, enhances peripheral glucose uptake, decreases fatty acid oxidation, and decreases absorption of glucose from the gastrointestinal tract.[8] Increased peripheral utilization of glucose may be due to improved insulin binding to insulin receptors.[9] AMPK probably also plays a role, as metformin administration increases AMPK activity in skeletal muscle.[10] AMPK is known to cause GLUT4 translocation, resulting in insulin-independent glucose uptake. Some metabolic actions of metformin do appear to occur by AMPK-independent mechanisms; a recent study found that “ the metabolic actions of metformin in the heart muscle can occur independent of changes in AMPK activity and may be mediated by p38 MAPK- and PKC-dependent mechanisms.”[11]

Metformin causes a few gastrointestinal side effects including nausea, metallic taste, diarrhea and abdominal discomfort[7] . These can be avoided if the dose is increased slowly, and taking the drug with meals. A small amount of weight loss, possibly due to drop in net caloric intake due to appetite repression and/or a reduction in hyperinsulinemia is suggested. Falling in the same drug class as phenformin, the reported incidence of lactic acidosis is surprisingly low, 0. 03 per 1000.

In a US double-blind clinical study of GLUCOPHAGE in patients with type 2 diabetes, a total of 141 patients received GLUCOPHAGE therapy (up to 2550 mg per day) and 145 patients received placebo.

### Most Common Adverse Reactions (> 5. 0 Percent) in a Placebo-Controlled Clinical Study of GLUCOPHAGE Monotherapy

The occurrence can further be avoided if contraindications are followed. It is contraindicated in people with a high risk of lactic acidosis: renal serum creatinine levels over 150 μmol/l[14}or hepatic impairment, respiratory insufficiency, severe infection and alcohol abuse. Any pharmacological therapy that alters either of the factors mentioned before is also considered. It should also be used cautiously in elderly especially those above 80 years of age. It is recommended to monitor renal function upon initiation and at least once a year thereafter.

It should be withheld immediately before a person has a procedure with a radiocontrast dye, as the dye increases the risk of renal failure and therefore lactic acidosis [15] [16]. It should also be discontinued before and surgery and can be started immediately after if the renal function is normal and the patient is stable. It is also recommended to monitor hematological parameters as it alters vitamin B12 absorption [12] [13] and therefore cause anemia (7% in clinical trials). The mechanism of action is unknown but can be reversed by discontinuation of the drug.

Daily dosage should be 500 mg orally twice daily with meals. The dose can be increased every 2 weeks to 2000 mg daily.

### References

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