

## Biguanides – Metformin

Metformin has been available in the UK since 1957. It is available in two forms:

- Immediate release (absorbed in the upper small bowel)
- Modified release (MR) (absorbed more slowly in the upper gut)

### Indication

For treatment of type 2 diabetes mellitus when dietary management and exercise alone do not result in adequate glycaemic control:

- In adults, as monotherapy or in combination with other oral glucose-lowering agents, or with insulin
- In children and adolescents aged 10 years and over, as monotherapy or in combination with insulin

### Mechanism of action

Complex mechanisms of action are still under review. These may include:

- Reduced liver glucose production by gluconeogenesis or glycogenolysis
- Increased insulin sensitivity in muscle, increasing peripheral glucose uptake
- Delay in absorption or increased usage of glucose in the intestine
- Alteration in the gut microbiome
- Possible effects increasing secretion of glucagon-like peptide-1

### Dosing and titration

Initial dose: 500mg once daily after your evening meal. Titrate according to tolerability by 500mg/day every two weeks, up to 1000mg twice daily.

Consider change to metformin MR if gastrointestinal side effects persist after two weeks of initiation/dose change.

A [patient information leaflet](#) can be given to patients.

### Contraindications

- Hypersensitivity to metformin or any excipients
- Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis)
- Diabetic pre-coma
- Severe renal failure (estimated Glomerular Filtration Rate (eGFR) less than 30 mL/min)
- Acute conditions with the potential to alter renal function such as: dehydration, severe infection, shock
- Disease which may cause tissue hypoxia (especially acute disease, or worsening of chronic disease) such as: decompensated heart failure, respiratory failure, recent myocardial infarction, shock
- Hepatic insufficiency, acute alcohol intoxication, alcoholism

## Cautions

- eGFR less than 60mL/min: Pause if iodine-containing contrast investigation or surgery planned. Check eGFR 48 hours later and restart if stable
- eGFR 30–45mL/min: Reduce dose to 1000 mg total daily

## Monitoring

Determine renal function before treatment and at least annually (at least twice a year in patients with additional risk factors for renal impairment, or if deterioration suspected).

## MHRA/Safety alerts

- [Metformin in pregnancy: study shows no safety concerns](#) (March 2022)
- [Metformin and reduced vitamin B12 levels: new advice for monitoring patients at risk](#) (June 2022)

## Noteworthy Interactions (Individual product license contains full list)

Drugs which may affect renal function (e.g. Non-Steroidal Anti-inflammatory drugs, Angiotensin Converting Enzyme (ACE) inhibitors, Angiotensin receptor blockers and diuretics, especially loop diuretics): monitor eGFR carefully.

## Information on adverse effects (Individual product license contains full list)

- **No** risk of hypoglycaemia (unless combined with other hypoglycaemic medication)
- **No** weight gain. Evidence of slight weight loss
- Gastro-Intestinal disturbance. Nausea, bloating, loose stools is common, when initiating therapy (but can happen at any time and is dose dependant). Slow titration advised if significant side effects. Switch to modified-release, which causes fewer side effects, if immediate-release not tolerated
- Lactic acidosis is rare, occurring in 3 to 10 per 100 000 person-years, but serious.
- Vitamin B12 deficiency due to malabsorption, which may also be associated with peripheral neuropathy if untreated
- Taste disturbance can occur
- Rare adverse effects include skin erythema, pruritus, urticaria, and hepatitis or abnormal liver function test

## Sick Day rules

Metformin should be stopped temporarily during periods of illness. Dehydration can make it more likely that lactic acidosis will develop. Patient to restart when they are well (normally after 24 to 48 hours of eating and drinking as usual). General [sick day rules](#) document contains further information.

## Blood Glucose Testing Strip Prescribing

### For patients prescribed metformin/gliptins/Sodium-glucose Cotransporter-2 Inhibitor (SGLT2i) only or in combination

Do not prescribe blood glucose strips for self monitoring unless short-term use advised by a specialist (e.g. when starting treatment with oral or intravenous corticosteroids or to confirm suspected hypoglycaemia). Advise patients can buy meters and blood glucose strips if they wish to.

## Counselling

Advice on dosing, titration, and sick day rules as above.

## References

- [A summary of oral diabetes medications 15<sup>th</sup> Edition June 2022](#) (Last accessed 05/09/2022)
- [BNF online](#) (Last accessed 05/09/2022)
- [NICE guideline \[NG28\] Type 2 diabetes in adults: management](#) (Last accessed 05/09/2022)
- [Prescribing Pearls: A guide to Metformin](#) (Last accessed 05/09/2022)
- [SPC for Metformin 500mg tablets \(Aurobindo Pharma\)](#) (Last accessed 05/09/2022)

## Document History

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