

Guideline on Metformin for Prevention of Antipsychotic-Induced Weight Gain



8 out of 10 will experience antipsychotic-induced weight gain

Low and normal BMI individuals are at a higher risk of clinically significant increases in weight

Choice of antipsychotic is the most important baseline risk factor at predicting antipsychotic-induced weight gain

Metformin is effective at preventing or treating antipsychotic-induced weight gain and improving cardiometabolic outcomes (unlicensed indication)

Lifestyle interventions (diet and exercise) should be provided to those taking antipsychotic medicine and continued if metformin is commenced



To be applied at antipsychotic initiation or following a switch from one antipsychotic to another

High risk
(Not first line)
Olanzapine
Clozapine

Medium risk
Quetiapine
Paliperidone
Risperidone

Lower risk
All other
antipsychotics

BMI ≥ 30
BMI 27-30 with one of the following:
Hypertension
Dyslipidaemia
Diabetes (Type 1 and 2)
Pre-diabetes
(HbA1c 42-47mmol/mol
Fasting glucose 6.1-6.9mmol/L)
Obstructive sleep apnoea

One of the following:
Hypertension
Dyslipidaemia
Diabetes (Type 1 and 2)
Pre-diabetes
(HbA1c 42-47mmol/mol
Fasting glucose 6.1-6.9mmol/L)
BMI >25 (Adjust for ethnicity)
Age 10-25

$>3\%$ weight gained at any
time during the first year
Adult: 60Kg + 3% = 1.8Kg
70Kg + 3% = 2.1Kg
80Kg + 3% = 2.4Kg
90Kg + 3% = 2.7Kg
Young Person: $>3\%$ weight
gained outside expected growth
trajectory

Co-commence metformin

Commence metformin

If unavailable

Commence GLP-1 Agonist



Avoid metformin with:

- Acute metabolic acidosis
- Severe renal failure (GFR < 30 mL/min)
- Hepatic insufficiency
- Acute physical illness or harmful use of alcohol - see 'When to stop' below



Useful information

- Metformin lowers appetite, lowers hepatic glucose production and improves insulin response
- It does not stimulate insulin secretion and so does not cause hypoglycaemia
- Metformin is a low cost medicine



Pre-treatment Monitoring

- Renal function (GFR)



Dose escalation

	Morning	Evening
Week 1	500mg	
Week 2	500mg	500mg
Week 4	1g	500mg
Week 6	1g	1g

Check for efficacy

- Take with or after food to minimise GI side-effects
- Target dose of 1-2g/day - BMI/weight or increases in appetite should inform dose escalation schedule
- Available as a slow release tablet once a day - could be considered if GI side-effects persist, twice daily dosing is likely to lead to poor adherence or if preferred by the individual
- Special considerations:
 - GFR 30-44mL/min = Max 1g/day



Side-effects

<1 in 10

- Transient - Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite
- Vitamin B12 decrease/deficiency

<1 in 100

- Taste disturbance

<1 in 10,000

- Lactic acidosis
- LFT abnormalities/hepatitis
- Skin reactions such as erythema, pruritus, urticaria



Ongoing Monitoring

- Weight/BMI
- Signs and symptoms of lactic acidosis - dyspnoea, muscle cramps, abdominal pain, hypothermia, or asthenia
- Liver function and HbA1c annually
- Renal function annually or 6 monthly for those >75 years or taking concomitant NSAIDs, ACE inhibitors, angiotensin II receptor antagonists and diuretics (especially loop diuretics)
- Vitamin B12 annually or 6 monthly for those with vegan diet, bariatric surgery, prescribed PPI or colchicine, older age or with gastrointestinal disorders affecting absorption - administer corrective treatment for vitamin B12 deficiency in line with current clinical guidelines; continue metformin therapy for as long as it is tolerated and not contraindicated



When to stop

- If lactic acidosis is suspected or if risks for lactic acidosis present - dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), acute alcohol intoxication, harmful use of alcohol, decompensated heart failure, respiratory failure, recent myocardial infarction, hypovolemic shock, severe infection
- Prior to or at the time of administration of iodinated contrast agents (restarted at least 48 hours after)
- If GFR drops below 30mL/min
- BMI <20
- Sick day rule - Stop if systemically unwell (restart when well)
- If antipsychotic is stopped