



**Wolverhampton
Diabetes Care**

What Care to Expect

Glycaemic Control Strategies for Type 2 Diabetes

Targets

- The objective of good glycaemic control is to achieve the lowest HbA1c or fasting blood glucose that can be safely attained without significant risk of hypoglycaemia aiming for HbA1c $\leq 7\%$ (DCCT) and fasting and pre-prandial blood glucose $\leq 7\text{mmol/l}$.

Diet, weight, exercise and lifestyle

Lifestyle changes are crucial cornerstones of therapy but as a monotherapy they rarely achieve target outcomes.

Oral hypoglycaemic agents

The metabolic abnormalities of Type 2 diabetes are progressive and there is a time-related need for increasing drug intervention.

Therapeutics and Concordance

To improve compliance, consider using once daily preparations in patients on more than four drugs. Drugs should be titrated to the targeted standard recommended doses.

Metformin

This is the first line agent at diagnosis: It is the only agent associated with decreased mortality. It is safe and has little hypoglycaemia risk. It should be prescribed from diagnosis in all patients suitable for tablet treatment if there are no relative or absolute contra-indications. Where a sulphonylurea has been used first line, Metformin is the standard second line agent.

Metformin contra-indications

- Known hypersensitivity to Metformin
- Renal insufficiency - serum creatinine $> 120\text{umol/l}$.
- Uncontrolled cardiac failure
- Acute haemodynamic compromise or hypoxic state
- Dehydration
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis
- Use of iodinated contrast for radiological examinations (withdraw on the day and for 48 hours after the procedure; restart once normal renal function is documented)
- Withdraw for 2 days before general anaesthesia and reinstate when renal function is stable
- Caution in elderly patient since serum creatinine may be a poor indicator of acute renal failure in this age group

Metformin relative contra-indications

- Marked hyperglycaemia at diagnosis (fasting blood glucose $> 15\text{mmol/l}$)
- Rapid weight loss with BMI $< 22\text{kg/m}^2$.

Metformin dose

Start at 500mg daily for at least 1 week, then 1 twice a day for at least 1 week, then 1 three times a day. UKPDS target dose was 850mg three times a day. Dose titration should be done slowly. Advise patients to take after food.

Insulin secretagogues

These include sulphonylureas (SU) and the newer rapid acting insulin secretagogues nateglinide and repaglinide.

- Insulin secretagogues should be used in combination with Metformin in normal, overweight or obese people when glucose control becomes unsatisfactory
- Insulin secretagogues should be considered as an option for 1st line therapy when:
 - Metformin is not tolerated or is contra-indicated
 - people with BMI ≤ 22
- The standard SU's are the insulin secretagogues of first choice
- Modern long acting once daily SU's are recommended to improve concordance with therapy e.g. Glimepiride
- Rapid acting insulin secretagogues (nateglinide and repaglinide) may have a role in attaining tight glucose control in patients with non-routine daily patterns but this is an infrequent indication. Tolbutamide is probably as effective as the drugs and a lot cheaper.
- Clinicians and those using any insulin secretagogues should be aware of the risk of hypoglycaemia and be alert to it.
- Where there is hypoglycaemia or there is a risk of, or need to avoid hypoglycaemia (e.g. drivers and those operating machinery) consider the use of a short acting sulphonylurea (Tolbutamide) or the rapid insulin secretagogues (Nateglinide or Repaglinide).

Glitazones

These should only be used in combination with Metformin or a sulphonylurea when there is intolerance or contraindicated to either of these two drugs. Their use in triple therapy should be under specialist supervision only. Both available drugs should be increased to a standard maintenance dose at 8 weeks since there is little risk of hypoglycaemia. Consider their earlier use instead of a sulphonylurea as first agent or second line with Metformin where sulphonylurea related hypoglycaemia may be seen as an unacceptable risk such as for occupational reasons e.g. professional driver. Monitor LFT's before treatment then every 2 months for 12 months then periodically thereafter.

Conversion to insulin

This should occur when oral hypoglycaemic agents are being used in a near maximal or maximal dose, without achieving acceptable glycaemic control (HbA1c < 7%). Convert to twice daily insulin. Stop oral agents at this stage.

Insulin and oral agent combination therapy

The only acceptable combination is insulin and Metformin. Generally stop all oral hypoglycaemic agents at insulin start up. Consider re-starting Metformin if significant weight gain (>3%) and/or poor control with high insulin doses (HbA1c > 7% and insulin > 2U/Kg). Only occasionally is it appropriate to continue Metformin at insulin start up in those obese patients (BMI > 30) with prior difficulty in controlling weight gain.

Drug	Caution	Start dose	Target / Maximal dose
Metformin	Elderly, cardiac / renal / hepatic impairment	500mg od	850 mg bd / 850mg tds
Glimepiride	Hypoglycaemia	1mg od	Step titrate to target HbA1c and blood glucose. Max dose 4mg/day
Gliclazide	Hypoglycaemia risk, bd dosing and high tablet count at maximal therapy.	40 mg od	Step titrate to target HbA1c and blood glucose. Max dose 160 mg o bd
Pioglitazone	Cardiac / renal / hepatic impairment, oedema	30mg od	30mg od
Rosiglitazone	Cardiac / renal / hepatic impairment, oedema	4mg od	8mg od