Appendix A: Drugs for diabetes during weight management

Weight loss is a potent treatment for type 2 diabetes: blood glucose falls during active weight loss, and often falls rapidly on starting TDR. Hypoglycaemia is possible without medication dose reduction or withdrawal. Requirement for insulin or other glucose-lowering drugs often falls rapidly but may rise somewhat when the patient has stabilized at a new lower weight.

Type 1 Diabetes, insulin dose requirement will fall, but never to zero.
Suggested management as follows:

- **On starting TDR**, reduce insulin doses to 75%.
- **During TDR** Monitor blood glucose (BG) frequently during weight loss, reducing the doses further in steps of 20% if BG falls to below 6 mmol/l before meals.
- **During Food Reintroduction and Weight Loss Maintenance.** When before-meal BG rises consistently above 6mmol/l, increase insulin doses by 2unit steps.

Type 2 Diabetes on insulin: insulin requirements will fall rapidly on TDR, sometimes to zero.
Management as follows:

- **On starting TDR,** reduce insulin doses to 75%.
- **During TDR** Monitor blood glucose frequently, when BG falls to below 6mmol/l before meals, reduce first to 50% of the initial dose, and then to 25%.
- **Stopping Insulin**: If blood glucose falls below 6mmol/l before meals on 25% of the original doses, insulin can usually safely be stopped. Continue monitoring blood glucose until insulin has been stopped for at least 2 days, and then check weekly until it is remaining normal, and primary diabetic symptoms have not recurred.
- **During Food Reintroduction and Weight Loss Maintenance.** If before-meal BG rises consistently above 6mmol/l
    a. Consider returning to TDR for 4 weeks, to achieve greater weight loss for sustained remission (some patients need to lose over 20kg).
    b. Introduce anti-diabetes medication which does not promote weight gain, according to usual guidelines (avoid sulphonylureas) **See order for reintroduction (below).**

Other anti-diabetic drugs

All anti-diabetic medications ***(Exceptions see below **)*** should be **stopped** on the day TDR is commenced, because blood glucose levels fall rapidly on the diet. This is a safety measure, to avoid hypoglycaemia, but also an important incentive to achieve remission.

- Monitor BG fasting each day initially, until clearly falling or stable.
- Where possible, measure fasting BG at each subsequent appointment
- If glycaemic control deteriorates, the usual explanation is poor adherence to dietary advice, and weight loss below expected: discuss resuming anti-diabetes medications
- If weight loss is satisfactory but blood glucose control is still inadequate, e.g. BGs consistently above 10mmol/l, consider reintroducing medication. **See order for reintroduction (below).**
    - Start at the lowest dose and increase gradually.
    - Subsequently, if control remains poor, add further agents
- Encourage and support efforts for further weight loss at each visit

***** Exceptions***

If diabetes improvement is the main aim, and remission considered less likely (e.g. > 10yrs duration of diabetes). All oral hypoglycaemic (sulphonylureas) drugs can still be stopped on the day TDR is commenced, and the patient managed as above. Some achieve remission after much longer durations. ***Patients receiving multiple medications for diabetes are less likely to achieve remission***. Blood glucose usually still falls with TDR, but It is safe to start TDR and remain on a drug which does not cause hypoglycaemia: metformin, glitazones, GLP-1 analogues, DPP-4 Inhibitors.

These drugs may become unnecessary after major weight loss. A therapeutic trial of drug withdrawal, monitoring BG over a few days, can be done either at the start of TDR, or later if weight loss is achieved. Stopping GLP-1 agonists may be less successful, as the patient may have more advanced diabetes, or be more dependent on the weight-loss effect of the drug.
These drugs have some small metabolic benefits for people with type 2 diabetes aside from glucose-lowering and assist with weight loss and maintenance. However, they are not licenced for these purposes without diabetes (this may change very soon: currently under review at SMC).

- **SGLT2 inhibitors (gliflozins)** must be stopped before starting TDR, because they can cause ketoacidosis.
- **Sulphonylureas or repaglinide/nateglinide** should be stopped because of higher risk of hypoglycaemia during TDR.
- **Statins**. There is no direct evidence over the withdrawal of statins, prescribed to reduce cardiovascular risks for people with type 2 diabetes, when there is remission of diabetes. These risks remain elevated in the 'prediabetes' range (HbA1c 43-48 mmol/mol), so statins should be continued.

Protocol for patients who have osmotic symptoms (thirst, polyurea) and/or pre-meal BG >10mmol/l (When these values are not falling with weight loss).

GP/PN/ Diabetic Nurse Practitioner (liaise with Counterweight Practitioner) to:

- Exclude intercurrent illness (e.g., viral infection, urinary tract infection etc.)
- Check HbA1c. (reflects blood glucose over previous 3 months)
- If weight loss is satisfactory (according to charts held by Counterweight Practitioner), re-introduce anti-diabetic medication, and increase dosage gradually (see below for suggested order of reintroduction of medications).
- Subsequently, if control remains poor, add further agents according to usual guidelines.

Counterweight Practitioner (liaise with GP/PN/ Diabetic Nurse Practitioner) to:

- Check if weight loss is as anticipated (see page 24 Counterweight-Plus Flipchart).
- If weight loss is below expected, discuss TDR compliance with the patient: re-check at next visit.
- If weight loss is adequate, refer to GP/PN

Order for reintroduction of anti-diabetic medications (may vary with national or local guidelines)

1. Reintroduce metformin (500mg bd). If this has previously not been tolerated for the individual, try the slow-release preparation. If needed, increase to 1g bd over 2-4 weeks.
1. If a second agent is required, add sitagliptin 100mg od.
2. If control is still inadequate, consider liraglutide, in a dose up to 3mg/day for optimal weight control
3. Add gliclazide, starting with 80mg od (or other sulphonylurea if preferred). **PLUS advice and support to avoid weight gain**
4. If glucose control remains inadequate, follow current guidelines. Insulin may be considered, **PLUS advice and support to avoid weight gain.**