Deprescribing in type 2 diabetes

Treatment intensification of glucose-lowering therapies can delay and prevent the long-term complications associated with type 2 diabetes. However, there may be circumstances where deprescribing of glucose-lowering therapies is required. This factsheet will focus on situations where deprescribing is deemed appropriate and will equip the reader to deprescribe non-insulin glucose-lowering therapies in a safe and patient-centred manner.

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Aim of deprescribing

The aim of deprescribing is to reduce overtreatment, treatment burden and risk of harm. Deprescribing is a **supervised process** and involves the following (Aubert et al, 2021):

- Stopping or reducing the dose of a glucose-lowering drug.
- Switching to an alternative glucose-lowering class with a more favourable risk–benefit ratio or lower risk of hypoglycaemia.
- Simplifying a medication regimen.
- Reduction in self-monitoring of blood glucose.
- Reduction in the frequency of diabetes-specific assessments (e.g. checking of urinary albumin:creatinine ratio).
- Cessation or reduction of blood pressure medications or statins.

Box 1 highlights the situations where deprescribing may be considered.

Box 1. Situations where deprescribing may be considered (Aubert et al, 2021).

- A person's HbA_{1c} falls below target as a result of lifestyle changes leading to weight reduction or increased effectiveness of treatment regimens.
- New onset of clinical conditions that lead to contraindications (e.g. pioglitazone use in heart failure).
- New/worsened onset of chronic kidney disease.
- Hypoglycaemia (especially in the frail/elderly).
- Treatment failure.
- Preference for a less intensive regimen due to adherence or tolerability issues or medication burden.
- Frailty and those who have low levels of support at home.
- Low cognitive function.
- Short life expectancy.

Individualising treatment targets

Although SIGN (2017) and NICE (2022) recommend HbA_{1c} treatment targets of ≤53 mmol/mol (48 mmol/mol at diagnosis) and ≤48 mmol/mol, respectively, HbA_{1c} treatment targets should be individualised and agreed with the patient. This requires a multifactorial approach depending on the patient and disease features such as coexisting comorbidities, risk of hypoglycaemia, life expectancy, duration of diabetes and motivation (Davies et al, 2022). See the ***Table*** alongside for recommended individualised HbA_{1c} and fasting blood glucose level targets (Aubert et al, 2021; Strain et al, 2018).

Health status	HbA_{1c} treatment target and fasting blood glucose targets	HbA_{1c} deprescribing threshold
Healthy, younger individuals with low hypoglycaemia risk	<53 mmol/mol 4–7 mmol/L	<42 mmol/mol
Healthy, older adult (>65 years)/pre-frail/mild frailty and functionally independent	<58 mmol/mol 5–7 mmol/L	<53 mmol/mol
Moderate to severe frailty, >2 comorbidities, reduced life expectancy or mild cognitive function	≤64 mmol/mol 6–8 mmol/L	<58 mmol/mol
Very severe frailty, significant comorbidity, limited life expectancy, moderate-to-severe cognitive impairment	≤70 mmol/mol 7–10 mmol/L	<64 mmol/mol
End of life/palliative care	Manage symptomatic hyperglycaemia	n/a

Tips on deprescribing effectively and safely

If deprescribing is deemed necessary:

- Stop or reduce doses of glucose-lowering drugs that can cause hypoglycaemia (e.g. sulfonylureas), especially if a person is experiencing hypoglycaemia.
- If the patient is on an SGLT2 inhibitor, consider continuing it, especially if they have other comorbidities including chronic kidney disease, heart failure or established cardiovascular disease, as they may benefit from continuing this class of drug.
  - ➤ However, the additional benefits of the class will need to be balanced with the risk of hypotension, mycotic genital infection and the need for the person to be able to implement sick day rules.
  - ➤ Ensure the person's eGFR is checked regularly to determine the SGLT2 inhibitor's safety and efficacy.
- Treatment should only continue if the person's individualised HbA_{1c} target has been achieved 3–6 months after starting the treatment, or there has been an HbA_{1c} reduction of 5.5 mmol/mol or more; otherwise, following review of adherence, treatment discontinuation and intensification of treatment with another therapy class should be considered (SIGN, 2017).

Deprescribing process

Deprescribing of glucose-lowering medicines should always be done following shared decision-making with the person or with their family/carer. When in doubt which glucose-lowering medicine should be deprescribed, the person could be asked their preference.

A tapering plan should be developed with the person or their family/carer to either stop the glucose-lowering drug, switch to another class or reduce the dose gradually over several weeks. In cases where a sulfonylurea dose has been reduced, increased frequency of blood glucose monitoring is required to ensure the deprescribing has been appropriate.

If the person has been experiencing hypoglycaemia, then dose reduction should continue until the hypoglycaemia resolves. If, following deprescribing, there is symptomatic hyperglycaemia or blood glucose levels rise above the individual's target, return to the previous dose or consider switching to an alternative drug class with a lower risk of hypoglycaemia.

At each stage, optimise diet and lifestyle measures, but bear in mind this does not apply to the frail and elderly. Refer to the ***Table*** below for the author's suggestions on the principles of dose adjustment of glucose-lowering drugs.

Follow-up

Following deprescribing, follow-up with the patient to check their HbA_{1c} or blood glucose levels is pertinent to ensure that deprescribing has not been detrimental to their glycaemic control. The clinician will need to ensure their practice has a good recall system in place.

As any HbA_{1c} changes will not be seen until after 3 months, the patient should be advised to monitor symptoms of hyperglycaemia (excessive thirst or urination, fatigue) if they do not have a blood glucose meter and are not on any glucose-lowering drugs that cause hypoglycaemia. Those who have been provided a glucose meter should monitor their blood glucose levels regularly. In both cases, the person should be advised to contact their diabetes healthcare team if they have any concerns.

Principles of reducing non-insulin glucose-lowering drug doses and monitoring requirements.

Drug or drug class	Hypo risk	Dose reduction	When and how often to monitor	Examples of situations where deprescribing is necessary
Metformin	Low	500–1000 mg every 3 months, if eGFR and/or HbA_{1c} allow	Monitor signs of hyperglycaemia. Check HbA_{1c} in 3 months	Adverse effects/tolerability; adherence; below-target HbA_{1c} due to lifestyle changes or effectiveness of treatment regimen; to reduce tablet burden; end of life; new onset of clinical conditions that lead to contraindications (e.g. acute unstable chronic heart failure or renal impairment)
Sulfonlyurea (e.g. gliclazide)	High	40–80 mg reduction at a time, guided by patient's blood glucose profile	Monitor fasting and pre-evening-meal blood glucose levels, and detitrate accordingly. Check HbA_{1c} in 3 months	Hypoglycaemia or risk of hypoglycaemia due to lifestyle changes or effectiveness of treatment regimen; no longer needed for rescue therapy or steroid-induced hyperglycaemia; to reduce tablet burden; treatment failure; frailty; end of life; low cognitive function; adherence; new onset of clinical conditions that lead to contraindications (e.g. severe renal or hepatic impairment)
Pioglitazone	Low	If at 45 mg, can reduce to 30 mg, then 15 mg, then stop; or stop immediately, especially if comorbidity arises and causes contraindication	Monitor signs of hyperglycaemia. Check HbA_{1c} in 3 months	Treatment failure; adverse effects; below-target HbA_{1c} due to lifestyle changes or effectiveness of treatment regimen; end of life; new onset of clinical conditions that lead to contraindications (e.g. uninvestigated macroscopic haematuria)
SGLT2 inhibitor	Low	Stop	Monitor signs of hyperglycaemia. Check HbA_{1c} in 3 months	Adverse effects/tolerability; adherence; new onset of clinical conditions that lead to contraindications (e.g. DKA); frailty; end of life
DPP-4 inhibitor	Low	Stop	Monitor signs of hyperglycaemia. Check HbA_{1c} in 3 months	Treatment failure; adverse effects; below-target HbA_{1c} due to lifestyle changes or effectiveness of treatment regimen; new onset of clinical conditions that lead to contraindications (e.g. pancreatitis); end of life
GLP-1 receptor agonist	Low	If on high dose, reduce to maintenance dose. Can stop completely but advise patient of potential risk of weight gain	Monitor signs of hyperglycaemia. Check HbA_{1c} in 3 months	Adverse effects/tolerability; adherence; below-target HbA_{1c} due to lifestyle changes or effectiveness of treatment regimen; treatment failure; frailty; end of life; new onset of clinical conditions that lead to contraindications (e.g. pancreatitis)

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