CKM Guidance

Cardiovascular-Kidney-Metabolic Disease

Preventing Adverse Outcomes in Cardiovascular Kidney Metabolic Conditions

Last content update date: 6th May 2026
File date: 13th June 2026
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Instructions:

The guidance is separated into the multiple sections.

Clicking on the yellow highlighted text will take you to the relevant section of the guidance on the guidance web site.

Clicking on a pink highlighted abbreviation will take you to the relevant abbreviation within the abbreviations section of this document.

Clicking on a blue link will open relevant external guidance in a new window for more detailed information.

Contents:

8. Management of hyperglycaemia in type 2 diabetes

Management of hyperglycaemia in type 2 diabetes

- This section provides a summary of recent changes in the management of type 2 diabetes, focusing on management relevant to CKM conditions only. Detailed guidance on the screening for diabetes, differentiating between the types of diabetes, and management of type 2 diabetes and its complications can be found here.
- Confirming the correct type of diabetes remains important for whānau with diabetes to access and receive best care.

Diagnosis of type 2 diabetes

- The diagnostic criteria for diabetes and prediabetes in Aotearoa New Zealand now aligns with the rest of the world:

- Diabetes
  - HbA1c ≥ 48 mmol/mol OR
  - Fasting glucose ≥ 7 mmol/L OR
  - 2 hour glucose > 11 mmol/L on a 75 g glucose tolerance test OR
  - Random blood glucose > 11 mmol/L if symptoms of diabetes
- Prediabetes
  - HbA1c 42 – 47 mmol/mol OR
  - Fasting glucose 6.1 – 6.9 mmol/L OR
  - 2 hour glucose 7.8 – 11 mmol/L on a 75 g glucose tolerance test

- The diagnosis of diabetes still requires two confirmatory tests unless the initial HbA1c is > 53 mmol/mol. If required, the 2nd confirmatory test should be done as soon as possible.

Treatment targets in type 2 diabetes

- HbA1c is the most common glycaemic treatment target in type 2 diabetes because continuous glucose monitoring is currently not funded for type 2 diabetes in Aotearoa
  - Target HbA1c for most is < 53 mmol/mol
  - Target HbA1c < 48 mmol/mol preferred in young adults and pre-pregnancy
  - Targets should always be balanced against risk of hypoglycaemia → **only insulin and sulphonylureas can cause significant hypoglycaemia**
  - **Target HbA1c 55 – 70 mmol/mol may be suitable if high risk of hypoglycaemia or tight glycaemia is not required e.g. life expectancy limited by other conditions**

- **Continuous glucose monitoring (CGM) can also be useful in type 2 diabetes, especially in high-risk groups, but is not currently funded.**

- High-risk groups with type 2 diabetes who will likely benefit from CGM:
  - Treatment with insulin and/or sulfonylureas
  - Youth and young adults
  - Pregnancy
  - On dialysis
  - Physical and/or cognitive impairment that prevents monitoring blood glucose levels

- Tips to increase access to CGM in type 2 diabetes include:
    - Discuss self-funding intermittent use of CGM
    - Using the disability allowance to fund CGM if able
    - Utilise free trials of CGM

- Important CGM targets include:
    - Time in range (TIR; % glucose levels 3.9 – 10 mmol/L) > 70%
        - Target TIR is > 80% if target HbA1c < 48 mmol/mol
    - Time below range (TBR; % glucose levels < 3.9 mmol/L) < 4% → only relevant if on insulin or sulfonylureas
    - Glucose management indicator (GMI) < 53 mmol/mol
        - Target GMI is < 48 mmol/mol if target HbA1c < 48 mmol/mol

Best choice of glucose lowering therapies in type 2 diabetes

Management of type 2 diabetes is now focused on preventing, delaying and reducing the progression of CV and renal disease and aiding weight loss if appropriate rather than just lowering glucose levels. Clinical inertia by health care professionals is still the greatest barrier to people with diabetes reaching their treatment targets. Comprehensive guidance on all aspects of the management of type 2 diabetes and how to reduce treatment inertia can be found here. **Key concepts in best choice of glucose lowering therapies includes:**

- Healthy living interventions are first line management and are important at all stages of type 2 diabetes → they are discussed in detail here
    - 10-15% total body weight loss (TBWL) is typically required to achieve remission of type 2 diabetes if increased adiposity, but even 5% TWBL will significantly improve glucose levels

- Metformin should be started at diagnosis if eGFR > 15 mL/min regardless of HbA1c
    - Metformin is often best tolerated starting at 250 – 500 mg with largest meal
    - Titrate metformin to 1 g twice daily or maximal tolerated dose
    - Metformin in combination tablets (e.g. Jardiamet, Galvumet) seems to be better tolerated than metformin alone
    - Doses of metformin need to be reduced once eGFR < 45 mL/min
    - GFR 30 – 44 mL/min → maximum metformin dose is 1 g daily
    - eGFR – 15 – 29 mL/min → maximum metformin dose is 500 mg daily
    - eGFR < 15 mL/min → stop metformin

- **If chronic kidney disease (UACR > 3 mg/mmol OR eGFR < 60 mL/min), heart failure, CVD OR high CV risk (5 year CV risk ≥ 10%) add empagliflozin OR a GLP1 receptor agonist (GLP1Ra) regardless of HbA1c**
    - Empagliflozin is typically preferred if heart failure or CKD predominate
        - Start 10 mg daily alone or in combination with metformin
        - Can increase to 25 mg daily if HbA1c remains above target
        - Glucose-lowering effects of empagliflozin reduce once eGFR < 30 mL/min but CV and renal protection persist
        - Empagliflozin can be started if eGFR > 20 mL/min and should only be stopped if adverse effects occur or dialysis is started.
        - Sick day advice and tips to reduce adverse effects should be provided
        - Withhold empagliflozin in acute illness and 3 days before (including day of) major surgery, bowel prep or low carb diet. Restart when well and eating and drinking normal.
        - Doses of sulfonylureas may need to be reduced by 50% and doses of insulin by approximately 20% to avoid hypoglycaemia when starting empagliflozin – typically only required if baseline HbA1c < 64 mmol/mol.
        - Discuss importance of genital hygiene and reporting changes or concerns
        - Do not use in pregnancy, breastfeeding or children < 10 years of age
        - Do not use in type 1 diabetes, significant alcohol intake, previous diabetic ketoacidosis (DKA) or low carbohydrate diets without specialist advice
        - If symptoms of DKA (e.g. nausea, vomiting, abdominal pain etc.) need to present to GP practice or A+E urgently to ensure blood ketones are < 1.5 mmol/L. DKA needs to be excluded if ketones > 1.5 mmol/L
    - GLP1Ra likely preferred if greater reduction in HbA1c and/or weight desired
        - Currently two funded injectable GLP1Ra for type 2 diabetes:
            - Dulaglutide 1.5 mg weekly → can increase to 3 mg and 4.5 mg weekly if HbA1c remains above target but beware potential for short supply
            - Liraglutide 0.6 mg daily → titrate to 1.8 mg daily or maximal tolerated dose
                - Need to prescribe BD fine 4 mm needles for injecting
        - Semaglutide is a more potent GLP1Ra and is well tolerated, but is not funded and costs approximately $480 – 500 per month

        - Start 0.25 mg weekly and increase the dose every 4 weeks to 0.5 mg weekly then 1 mg weekly then 1.7 mg weekly then 2.4 mg weekly or maximal tolerated dose

    - Discuss strategies on how to reduce adverse effects
        - Ensure adequate hydration and stop eating when feeling full
        - Eat smaller meals and avoid alcohol, fatty and spicy foods
        - Slow down dose increases if GI adverse effects
        - GI adverse effects typically dissipate within 2-3 weeks
        - Doses of sulfonylureas may need to be reduced by 50% and doses of insulin by approximately 20% to avoid hypoglycaemia when starting GLPRa – typically only required if baseline HbA1c < 64 mmol/mol
        - Do not use in pregnancy, breastfeeding or children < 10 years
            - GLP1Ra should be stopped once eGFR < 15 mL/min

- Dual empagliflozin/GLP1Ra therapy is typically preferred if HbA1c remains above target on either agent alone. **There is a mismatch between best practice and the special authority criteria**, which states the patient must have heart failure (empagliflozin) or an HbA1c > 53 mmol/mol (both empagliflozin and GLP1Ra) if no heart failure.
    - Dual therapy can only be fully funded with GLP1Ra under the diabetes special authority and empagliflozin under the heart failure special authority.
    - Self-funding of these agents should be offered but are expensive (approximately $85 per month for empagliflozin and minimum $250 per month for GLP1Ra). Tips to increase access include:
        - Ensuring empagliflozin is funded under the heart failure criteria if applicable
        - Funding the GLP1Ra under the diabetes special authority due to the much greater cost
        - Utilising the disability allowance to cover the cost of empagliflozin if able
        - Prescribing half a 25 mg tablet of empagliflozin or 1 tablet of empagliflozin 12.5 mg with metformin to halve the cost to approximately $43 per month – please note this is off-label.
        - Checking the cost between pharmacies because there continues to be wide variation

- Pioglitazone is likely the next best agent if HbA1c remains above target if no contraindications
    - History of bladder cancer

        - High risk of fractures – especially if known osteoporosis
        - Peripheral oedema e.g. uncontrolled heart failure
        - Pioglitazone now appears safe in macular oedema but best to withhold if severe macular oedema undergoing treatment
        - Pregnancy or breastfeeding
        - Start 15 mg daily → it may take up to 16 weeks before the full effects on HbA1c are seen but can titrate up to 45 mg daily as required

- **If no renal or CV disease and 5 year CV risk < 10% then treatment is added (not switched) if HbA1c is above target:**
    - If weight loss desired → empagliflozin and/or GLP1Ra preferred. Consider acarbose if HbA1c still above target but beware of adverse GI effects.
    - If weight loss not desired → consider vildagliptin (typically weight neutral and redundant if on GLP1Ra) and pioglitazone (may cause minimal weight gain)
        - Usual dose of vildagliptin is 50 mg twice daily either alone or in combination with metformin.
        - Maximum dose is 50 mg daily once eGFR < 50 mL/min

- **If HbA1c remains above target then consider sulfonylureas and insulin but beware risks of hypoglycaemia and weight gain**. These risks can be reduced by:
    - Using sulfonylureas first as the risks with sulfonylureas are minimal
    - Reinforcing healthy eating and dietitian input
    - Regular monitoring of glucose levels and consider CGM
    - Maximising other glucose lowering therapies so only lowest doses of sulfonylureas and insulin are required.
    - Ensuring all patients have an up to date sick day management plan
    - Reducing doses of sulfonylureas and insulin with declining renal function
    - Adding in prandial insulin rather than increasing basal insulin if the HbA1c is above target once doses of basal insulin reach 0.5 units/kg per day
    - Reducing doses of sulfonylureas by ≥ 50% and insulin by ≥ 20% if episodes of hypoglycaemia are occurring

Other important practice points in managing type 2 diabetes

- Intervening early in type 2 diabetes is important to increase chances of remission, slow progression of diabetes and prevent long term complications

    - Chances of remission of type 2 diabetes greatly decrease > 6 years post diagnosis
    - Diabetes continues to be the most common cause of visual loss, amputation, dialysis and renal transplant in Aotearoa New Zealand despite end-stage complications being largely preventable.

- Addressing inequities are critical in type 2 diabetes
    - Prevalence of type 2 diabetes is 1.4 to 3 times higher in Māori, Pacific peoples, and people from Indo-Asia.
    - Complications of diabetes are up to 3 to 5 times higher in these populations than Pākehā with diabetes.
    - Consider cultural supports early to address any barriers to diagnosis and management.
    - Aim for whānau-based care if possible and integrate care with Rongoā Māori practitioners if whānau wish

- Ideally HbA1c should be measured 3 monthly if above target with escalation of therapy as required. Once to target, HbA1c should ideally be measured 6 monthly as type 2 diabetes is a progressive disease.
- Smoking cessation and optimising management of blood pressure and dyslipidaemia are likely at least as important as optimising glucose levels in preventing, delaying and slowing complications of diabetes.
- The annual diabetes review continues to be important opportunity to optimise care including acting on results from the following:
    - Consideration whether treatment targets are appropriate if change in clinical circumstances
    - Performing a neurovascular examination of the feet and ensuring foot cares if increased risk
    - Ensuring retinal photoscreening is being performed at least 2-3 yearly
    - Screening for depression → the PHQ-2 score can be a useful screening tool
        - Scores ≥ 3 should prompt further screening with PHQ-9 or other tools
    - Screening for diabetes distress → the DDS2 score is a useful screening tool
        - Scores ≥ 3 highlight need to fully evaluate diabetes distress and consider support as appropriate
    - Calculating CV risk using the CKM risk assessment and management (CKM-RAM) calculator
    - Ensuring vaccinations and screening for malignancy is up to date
    - Screening for dental and periodontal disease
    - Discussing contraception and planning pregnancy in women and men of child bearing age

        - Glycaemia to target is also important in potential fathers

    - **NB:** The annual diabetes review does not have to be performed all in one appointment and different components may be split across the year

- Development of either a microvascular diabetic complication (e.g. diabetic eye, kidney or foot disease) or macrovascular diabetic complication (e.g. coronary artery disease) requires management as per high risk CKM conditions and high CV risk to prevent progression of the complication(s). These treatment targets include:
    - Adding empagliflozin or GLP1Ra regardless of HbA1c
    - ACEi or ARB if CKD or heart failure and no concerns over hypotension
    - Systolic BP 120 – 129 mmHg or lowest reasonably safely achievable BP
    - LDLc < 1.4 mmol/L
    - Serum urate < 0.36 mmol/L if gout (< 0.3 mmol/L if tophi)
    - Aspirin if previous CV event
        - NB: The risks of aspirin appear to outweigh the benefits for primary prevention of CV events in people with diabetes

- Neuropathic pain is common in people with diabetes and can usually be successfully treated
    - Mild pain → paracetamol
    - Moderate to severe pain → low dose tricyclic e.g. nortriptyline 10 mg nocte
        - Can titrate nortriptyline and add pregabalin or gabapentin as required
        - Pregabalin is typically more effective than gabapentin with less adverse effects in diabetic neuropathy
        - Carbamazepine can be added in severe cases
    - Topical capsaicin 0.075% may be useful for localised neuropathic pain
    - Diabetic neuropathic pain is typically not responsive to NSAIDs or opiates
    - Supportive footwear and early involvement of podiatry if foot disease is important

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↑ Back to contents

Abbreviations:

CKM
Cardiovascular-Kidney-Metabolic

↑ Back to contents

↑ Back to top