CKM Guidance

Cardiovascular-Kidney-Metabolic Disease

Preventing Adverse Outcomes in Cardiovascular Kidney Metabolic Conditions

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Please make sure to periodically check for updated content.

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.

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7. Management of hyperglycaemia in type 2 diabetes

- Management of type 2 diabetes is now focussed on preventing, delaying and reducing the progression of CV and renal disease and aiding weight loss if overweight rather than just lowering glucose levels. As a result, there are new key treatment concepts:
    - Lifestyle management and metformin are recommended for all with type 2 diabetes regardless of HbA1c
        - 10-15% total body weight loss (TBWL) is typically required to achieve remission of type 2 diabetes if increased fat mass, but 5% TWBL will significantly improve glucose levels
    - If renal disease (UACR > 3 mg/mmol OR eGFR < 60 mL/min), heart failure, CVD OR equivalent risk (5 year CV risk ≥ 10%) add empagliflozin OR a GLP1 receptor agonist (GLP1Ra) regardless of HbA1c

        - There is a mismatch between best practice and the special authority criteria for empagliflozin and GLP1Ra, which states the patient must have heart failure (empagliflozin) or an HbA1c > 53 mmol/mol (both empagliflozin and GLP1Ra) if no heart failure. Self-funding of these agents should be offered but are expensive (approximately $85 per month for empagliflozin and minimum $450 per month for GLP1Ra). Tips to access increase access include:
            - Using the heart failure special authority for empagliflozin if applicable
            - Funding the GLP1Ra under special authority if dual therapy due to the much greater cost
            - Utilising the disability allowance to cover the cost of empagliflozin if able
            - Prescribing half the 25 mg tablet of empagliflozin or 1 tablet of empagliflozin 12.5 mg with metformin (Jardiamet) 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
        - Empagliflozin is typically preferred if heart failure or renal disease predominate
        - GLP1Ra may be preferred if significant reduction in HbA1c and/or weight desired
        - Dual empagliflozin/GLP1Ra therapy preferred if HbA1c remains above target on either agent alone. Tips for allowing funded dual therapy include:
            - Using the heart failure special authority for empagliflozin if applicable
            - Funding the GLP1Ra under special authority if dual therapy due to the much greater cost
            - Utilising the disability allowance to cover the cost of empagliflozin if able
            - Prescribing half the 25 mg tablet of empagliflozin or 1 tablet of empagliflozin 12.5 mg with metformin (Jardiamet) 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
        - If HbA1c still above target then adding pioglitazone should be considered before other glucose lowering therapies.

    - 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.
        - If weight loss not desired → consider vildagliptin (typically weight neutral and redundant if on GLP1Ra) and pioglitazone (may cause minimal weight gain)

    - Sulfonylureas and insulin are still important treatment options but are often used last due to their risk of hypoglycaemia and weight gain (risk is much less for sulfonylureas).
    - Target HbA1c for most is < 53 mmol/mol
        - Target HbA1c < 48 mmol/mol preferred in young adults and pre-pregnancy
        - 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
        - **NB:** Targets should always be balanced against risk of hypoglycaemia, **but only insulin and sulphonylureas can cause significant hypoglycaemia**

- Comprehensive guidance on all aspects of the management of type 2 diabetes can be found here. Relevant links to specific areas of the guidance are included in the key points below on starting glucose lowering therapies in CKM:
    - Lifestyle management is important at all stages of type 2 diabetes and CKM disease
    - Metformin is often best tolerated if started at 250 mg – 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
            - eGFR 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
    - Empagliflozin is typically started at 10 mg daily alone (Jardiance) or in combination with metformin (Jardiamet)
        - 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 but should be stopped if adverse effects occur or dialysis is started.
            - Sick day advice and tips to reduce adverse effects should be provided for all:

- 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.

◦ Liraglutide is the only currently funded GLP1Ra for new starts

- Start 0.6 mg daily and titrate to 1.8 mg daily or maximal tolerated dose
- Dulaglutide (Trulicity) is still funded if previously funded under special authority
  - Typical dose is 1.5 mg weekly but may be increased to 3 mg and then 4.5 mg weekly if HbA1c remains above target
  - Semaglutide (Wegovy) and Tirzepatide (Mounjaro) will shortly be available and typically lead to greater weight loss and CV protection than older GLP1Ra but are not funded
    - Semaglutide can be started at 0.25 mg weekly and increased slowly to 2.4 mg weekly or maximal tolerated dose
    - Tirzepatide can be started at 2.5 mg weekly and increased slowly to 15 mg weekly or maximal tolerated dose
  - Tips should be provided 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 of age
        - GLP1Ra should be stopped once eGFR < 15 mL/min

    - Pioglitazone is started at 15 mg daily if no contraindications
        - Pioglitazone should not be used if history of bladder cancer, high risk of fractures (e.g. osteoporosis) or oedematous conditions (e.g. uncontrolled heart failure and actively treated macular oedema etc.)
        - It may take 16 weeks before the full effects on HbA1c are seen, but pioglitazone may be titrated up to 45 mg as required

- ***The guidance in this section is based on the National Type 2 Diabetes Management Guidance that was developed by the New Zealand Society for the Study of Diabetes (NZSSD) and the Ministry of Health, which can be accessed at www.t2dm.nzssd.org.nz. Our national diabetes guidance is largely based on the joint American Diabetes Association (ADA)/European Association for the Study of Diabetes (EASD) guidelines, which can be accessed at https://link.springer.com/article/10.1007/s00125-022-05787-2.***

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Abbreviations:

CKM
Cardiovascular-Kidney-Metabolic

CV
Cardiovascular

CVD
Cardiovascular Disease

DKA
Diabetic Ketoacidosis

eGFR
Estimated Glomerular Filtration Rate

GI
Gastrointestinal

GLP1Ra
Glucagon-Like Peptide-1 Receptor Agonists

GP
General Practitioner

HbA1c
Glycated Haemoglobin

TBWL
Total Body Weight Loss

UACR
Urinary Albumin:Creatinine Ratio

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