Therapeutic Guidelines

Algorithm for antihyperglycaemic treatment for adults with type 2 diabetes [NB1]

Patient with type 2 diabetes

At diagnosis, does the patient have any of the following features:

- severe hyperglycaemia (eg BGC more than 20 mmol/L)
- HbA1c more than 86 mmol/mol (10%)
- metabolic decompensation (eg diabetic ketoacidosis or hyperosmolar hyperglycaemia)?

NO

Start lifestyle modification (dietary changes and increased physical activity) and continue these lifelong [NB2].

Start metformin as first-line therapy, unless contraindicated or not tolerated, and increase to maximum tolerated dose [NB3].

Consider the HbA1c at diagnosis and set individualised glycaemic targets.

YES

For management of first presentation of severe hyperglycaemia in adults, see *Therapeutic Guidelines*.

Is the patient's HbA1c significantly above their individualised target at diagnosis (eg more than 16 mmol/mol [1.5%] above target)? [NB4]

NO

Independent of glycaemic management, consider adding an antihyperglycaemic drug with proven cardiovascular or renal benefit in patients with [NB5]:

- **atherosclerotic CVD** (established or a high risk of [NB6])—a GLP-1 receptor agonist (dulaglutide, liraglutide or semaglutide) OR an SGLT2 inhibitor (dapagliflozin or empagliflozin)
- **heart failure**—an SGLT2 inhibitor (dapagliflozin or empagliflozin)
- **CKD** [NB7]—an SGLT2 inhibitor (preferred) (dapagliflozin or empagliflozin) OR a GLP-1 receptor agonist (dulaglutide, liraglutide or semaglutide).

For more information on use of antihyperglycaemic drugs for cardiovascular and renal benefits, see *Therapeutic Guidelines*.

YES

At diagnosis, start a second antihyperglycaemic drug.

After 3 months of treatment, repeat HbA1c and consider other glycaemic parameters. Have the patient's individualised glycaemic targets been achieved?

YES

NO

Add another antihyperglycaemic drug [NB8].

cont. next page

Continue to:

- regularly review the efficacy, tolerability, complexity and cost of the patient's antihyperglycaemic drug regimen
- assess and manage other comorbidities or treatments impacting the patient's glycaemic profile
- check adherence, patient understanding and self-management
- reinforce the need to continue lifestyle modification.

For suggested monitoring of the glycaemic profile, see *Therapeutic Guidelines*.

Independent of glycaemic management, consider adding or changing a drug in the current regimen to an SGLT2 inhibitor or a GLP-1 receptor agonist with proven cardiovascular or renal benefit in patients with atherosclerotic CVD (established or a high risk of [NB6]), heart failure or CKD [NB7], if not already used [NB5]. For more information on use of antihyperglycaemic drugs for cardiovascular and renal benefits, see *Therapeutic Guidelines*.

Choice of additional antihyperglycaemic drug

For detailed considerations on drug choice (eg efficacy in HbA1c reduction, risk of hypoglycaemia, effect on weight, cardiovascular and renal benefits), see *Therapeutic Guidelines*.

For **patients with atherosclerotic CVD** (established or a high risk of [NB6]), **heart failure** or **CKD** [NB7], prioritise choosing an SGLT2 inhibitor or a GLP-1 receptor agonist with proven cardiovascular or renal benefit.

For **patients without these comorbidities**, usually choose an SGLT2 inhibitor, a DPP-4 inhibitor or a GLP-1 receptor agonist, but a sulfonylurea or insulin may also be used. Less common alternatives are acarbose or pioglitazone.

After 3 months, repeat HbA1c and consider other glycaemic parameters. Have the patient's individualised glycaemic targets been achieved? [NB9]

YES

NO

Further antihyperglycaemic therapy may involve adding another drug or changing a drug in the current regimen [NB8]. Three or more drugs may be needed to achieve and maintain glycaemic targets.

Choice of further antihyperglycaemic drug is:

- usually an SGLT2 inhibitor, a DPP-4 inhibitor, a GLP-1 receptor agonist, a sulfonylurea or insulin
- less commonly, acarbose or pioglitazone.

Do not delay starting injectable therapy (a GLP-1 receptor agonist or insulin) if glycaemic targets have not been achieved with oral drugs and the patient's HbA1c remains above 64 mmol/mol (8%).

For detailed considerations on drug choice (eg efficacy in HbA1c reduction, risk of hypoglycaemia, effect on weight, cardiovascular and renal benefits), see *Therapeutic Guidelines*.

Consider stopping any drug (other than metformin and insulin) that has not reduced HbA1c by at least 5.5 mmol/mol (0.5%) at optimal dosing, unless indicated for nonglycaemic benefits. For information on use of antihyperglycaemic drugs for cardiovascular and renal benefits, see *Therapeutic Guidelines*.

When a change in therapy is made, monitor response by measuring HbA1c after 3 months [NB9].

The ultimate regimen is likely to be either a mixed insulin regimen or bolus insulin added to a basal insulin regimen (with bolus doses before one or more meals) PLUS metformin PLUS an SGLT2 inhibitor or a GLP-1 receptor agonist.

Have the patient's individualised glycaemic targets been achieved?

YES

NO

Seek specialist advice.

Algorithm for antihyperglycaemic treatment for adults with type 2 diabetes [NB1] (cont.)

BGC = blood glucose concentration; CKD = chronic kidney disease; CVD = cardiovascular disease; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; HbA1c = glycated haemoglobin; SGLT2 = sodium-glucose co-transporter 2

NB1: See the Australian Therapeutic Goods Administration (TGA) website <www.tga.gov.au> for current approved indications and fixed-dose combination formulations of antihyperglycaemic drugs. Recommended combinations may not be subsidised on the Pharmaceutical Benefits Scheme (PBS). Not all single and fixed-dose combination antihyperglycaemic formulations are available on the PBS; see the PBS website <www.pbs.gov.au> for current information.

NB2: In addition to lifestyle modification, consider the need for intensive weight management with drug therapy or metabolic (bariatric) surgery—remission of type 2 diabetes may be possible with significant weight loss. For comprehensive information on management of obesity, see the Australian Obesity Management Algorithm, available on the Australian Diabetes Society website <diabetessociety.com.au/position-statements.asp>.

NB3: If metformin is contraindicated or not tolerated, choose an alternative antihyperglycaemic drug (eg an SGLT2 inhibitor, a DPP-4 inhibitor, or a sulfonylurea); the considerations when choosing an alternative drug to metformin for first-line therapy of type 2 diabetes in adults are the same as the #[considerations when adding or changing antihyperglycaemic drugs to improve glycaemic management].

NB4: For patients who do not have an HbA1c significantly above their individualised target at diagnosis, but have a high blood glucose concentration (eg 14 to 20 mmol/L) at diagnosis, consider starting a second antihyperglycaemic drug at diagnosis (in addition to lifestyle modification and metformin), as recommended for patients who have an HbA1c significantly above their individualised target.

NB5: At the time of writing, GLP-1 receptor agonists and SGLT2 inhibitors are not subsidised on the PBS specifically for their cardiovascular or renal benefits, except for dapagliflozin for heart failure; see the PBS website <www.pbs.gov.au> for current information.

NB6: To assess the risk of atherosclerotic cardiovascular disease (CVD), see Who should have their absolute cardiovascular disease risk estimated in *Therapeutic Guidelines*.

NB7: Chronic kidney disease (CKD) is defined as an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m^2 or established albuminuria.

NB8: When considering adding or changing an antihyperglycaemic drug, consider all aspects of the glycaemic profile (eg symptoms of hyperglycaemia, episodes of hypoglycaemia, hypoglycaemia unawareness); assess and manage other comorbidities or treatments impacting the patient's glycaemic profile; check adherence, patient understanding and self-management; and reinforce the need to continue lifestyle modification.

NB9: Once-weekly GLP-1 receptor agonists (dulaglutide and semaglutide) take 4 to 5 weeks to reach steady state and further improvement in HbA1c may be seen after the initial 3 months.

Published in *Therapeutic Guidelines*, August 2022.