National Diabetes Services Scheme
An Australian Government Initiative

AUSTRALIAN TYPE 2 DIABETES GLYCAEMIC MANAGEMENT ALGORITHM

This Type 2 Diabetes Glycaemic Management Algorithm should be read in conjunction with the Living Evidence Guidelines in Diabetes (please click here).

All patients should receive education regarding lifestyle measures: healthy diet, physical activity and weight management.

Determine the individual's HbA1c target – commonly ≤53 mmol/mol (7.0%) but should be appropriately individualised (refer to ADS position statement).

Weight loss of ≥10% will likely allow a reduction or cessation of glucose lowering medication. Consider intensive weight management options including:

- Low energy or very low energy diets with meal replacements
- Pharmacotherapy
- Bariatric surgery.

Click here for the Australian Obesity Management Algorithm

Review treatment: if not at target HbA1c or if presence of cardiovascular/chronic kidney disease –

- Check patient understanding of self-management including drug treatment
- Ensure current therapies are clinically appropriate including comorbidities/ therapies impacting glycaemic control
- Review medication adherence
- Assess tolerability, adverse effects and risk of interactions

Review treatment in 3 months. **If HbA1c not at target:** Reinforce lifestyle measures and review weight management strategies.

MONOTHERAPY: Metformin is the usual monotherapy unless contraindicated or not tolerated

Metformin | **SU** | **Insulin**

Less commonly used: acarbose, DPP-4 inhibitor, SGLT2 inhibitor GLP-1RA, or TZD. Only acarbose is PBS reimbursed for monotherapy.

DUAL THERAPY: Choice of treatment – add on an oral agent or injectable therapy

Choice of dual therapy should be guided by clinical considerations (presence of, or high risk of, cardiovascular disease, heart failure, chronic kidney disease, hypoglycaemia risk, obesity), side effect profile, contraindications and cost.

SGLT2 inhibitor | **GLP-1RA*** | **DPP-4 inhibitor** | **SU** | **Insulin**

Less commonly used are: acarbose or TZD.

MULTIPLE THERAPIES: Choice of treatment : include additional oral agent or GLP-1 RA or insulin

Choice of agents should be guided by clinical considerations as above. Note: combinations not approved by PBS include GLP-1RA with SGLT2i. Consider reviewing any previous medication that has not reduced HbA1c by ≥0.5% after 3 months and take into consideration **glycaemic AND non-glycaemic benefits.**

SGLT2 inhibitor | **GLP-1RA** | **DPP-4 inhibitor** | **SU** | **Insulin**

Less commonly used are: acarbose or TZD.

THEN...

To intensify treatment to meet glycaemic targets

- If on metformin+SU+DPP-4i, consider *adding* SGLT2i, or *switching* DPP-4i to a GLP-1RA, or an SGLT2i.
- When adding incretin therapy, use either a DPP4i or GLP-1RA (not both together).
- If on basal insulin, consider *adding* SGLT2i or GLP-1RA or bolus insulin with meals, or *change* to premixed/coformulated insulin.
- If on metformin+DPP4i+SGLT2i *consider* adding SU or insulin.

With increasing clinical complexity consider specialist endocrinology consultation

***Combinations not approved by PBS include GLP-1RA with SGLT2i. Use of PBS-subsidised GLP-1 RAs in combination with an SGLT2i is permitted when the SGLT2i is prescribed for an indication other than T2D (e.g. chronic kidney disease or heart failure). PBS-subsidised GLP-1 RA can only be commenced if SGLT2i has not achieved a clinically meaningful glycaemic response or if there is a contraindication/intolerance to an SGLT2i. PBS-subsidised GLP-1RA can only be combined with PBS-subsidised SGLT2i if the SGLT2i is being prescribed through the heart failure or CKD PBS code. Consider reviewing any previous medication that has not reduced HbA1c by ≥0.5% after 3 months, and consider glycaemic AND non-glycaemic benefits.**

- *Recommendation for* addition of a SGLT2i (or GLP-1RA where SGLT2i is not tolerated or contraindicated) to other glucose lowering medication(s) in adults with type 2 diabetes who also have cardiovascular disease, multiple cardiovascular risk factors and/or kidney disease.
- *Conditional recommendation for* metformin as first-line monotherapy in adults with type 2 diabetes.
- *Conditional recommendation for* DPP-4i addition to other glucose lowering medication(s) in adults with type 2 diabetes who have cardiovascular disease, multiple cardiovascular risk factors and/or kidney disease, and are unable to be prescribed an SGLT2i or a GLP-1RA due to either intolerance or contraindication.

For more details click here to access the Living Evidence Guidelines in Diabetes.

- *Conditional recommendation against* sulphonylurea being first choice medication to add tometformin as dual therapy as it may increase risk of hypoglycaemia.
- Dark blue boxes indicate usual therapeutic strategy (order is not meant to denote any specific preference); usual refers to commonly available, evidence based, cost effective therapy.
- Light blue boxes denote alternate approaches (order is not meant to denote any specific preference).
- White boxes indicate less commonly used approaches.

PBS = Pharmaceutical Benefits Scheme, HF = heart failure, CKD = chronic kidney disease, SU = sulfonylurea, TZD = thiazolidinedione, DPP-4i = dipeptidyl peptidase-4 inhibitor, GLP-1RA = glucagon like peptide-1 receptor agonist, SGLT2i = sodium glucose co-transporter inhibitor.

ads Australian Diabetes Society

diabetes australia

AUSTRALIAN TYPE 2 DIABETES MANAGEMENT ALGORITHM

Table of Evidence and Properties of Glucose-Lowering Agents†

Glucose-lowering Class and Drugs	Mechanism of Action	Outcome data	Contraindications	Precautions, Side Effects and Administration	Cost* and Accessibility
Biguanide • metformin • metformin XR	Reduces hepatic glucose output, lowers fasting glucose levels	**UKPDS**[1]	Renal impairment (eGFR<30 ml/min/1.73m^2) Severe hepatic impairment	**Precautions** Suspend treatment during acute disease/ conditions with the potential to cause tissue hypoxia or alter renal function. **Side Effects** GI side effects, lactic acidosis, weight neutral **Administration** Oral Start at low dose and up-titrate Slow release preparations available	General schedule on PBS **$**
Sulfonylureas • glibenclamide • gliclazide • gliclazide MR • glimepiride • glipizide	Triggers insulin release in a glucose-independent manner	**UKPDS**[2] **ADVANCE**[3] - Gliclazide MR	Severe renal or hepatic impairment	**Precautions** Hypoglycaemia **Side Effects** Weight gain **Administration** Oral Start at low dose and up-titrate Slow release preparation available	General schedule on PBS **$**
Dipeptidylpeptidase-4 (DPP-4) inhibitors • alogliptin • linagliptin • saxagliptin • sitagliptin • vildagliptin	Decreases inactivation of glucagon-like peptide (GLP-1) thereby increasing its availability. GLP-1 stimulates beta cell insulin release.	**EXAMINE**[4,5] - Alogliptin **SAVOR-TIMI 53**[6,7] - Saxagliptin **TECOS**[8] - Sitagliptin **CARMELINA**[9] - Linagliptin **CAROLINA**[10] - Linagliptin vs Glimepiride	Pancreatitis[11] Hospitalisation due to heart failure with saxagliptin[6]	**Precautions** Nasopharyngitis-often subsides in 10-14 days **Side Effects** Rash, pancreatitis, GI disturbances, weight neutral **Administration** Oral Dosage adjustment in renal impairment (except linagliptin)[12]	Alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin are PBS subsidised for use with either metformin or sulfonylurea (i.e. dual therapy) **$$** Alogliptin, linagliptin, saxagliptin, sitagliptin and vildagliptin are PBS subsidised for use with metformin and sulfonylurea (i.e. triple therapy) If on any DPP4i plus metformin, addition of dapagliflozin, empagliflozin or ertugliflozin (i.e. triple therapy) is PBS subsidised Alogliptin, linagliptin, saxagliptin, sitagliptin and vildagliptin are PBS subsidised for use with insulin
Thiazolidinediones (TZD) • pioglitazone • rosiglitazone is not available in Australia	Transcription factor peroxisome proliferator-activated receptor gamma agonists. Durably lowers glucose levels through insulin sensitisation.	**PROACTIVE**[13] - Pioglitazone **RECORD**[14] - Rosiglitazone		**Precautions** Symptomatic heart failure **Side Effects** Fluid retention, heart failure, increased risk of non-axial fractures in women, increased risk of bladder cancer, weight gain **Administration** Oral	PBS subsidised for use in combination with metformin or sulfonylurea or both **$$** Patient must have a contraindication or intolerance to metformin- sulfonylurea combination PBS subsidised for use with insulin
Alpha 1 glucosidase inhibitors • acarbose	Slows intestinal carbohydrate absorption and reduces postprandial glucose levels		Severe renal impairment (creatinine clearance < 25 ml/min/1.73m^2)	**Precautions** Gastrointestinal disorders associated with malabsorption **Side effects** Bloating and flatulence, weight neutral **Administration** Oral Take with meals as tolerated	General schedule on PBS **$**
Sodium-glucose co-transporter-2 (SGLT2) inhibitors • dapagliflozin • empagliflozin • ertugliflozin	Inhibits a Sodium-glucose cotransporter to induce urinary glucose loss and decrease blood glucose levels Non-glycaemic benefits shown in heart failure and CKD still to be defined	**DECLARE**[15] - Dapagliflozin **DAPA-HF**[16] - Dapagliflozin **DAPA-CKD**[17] - Dapagliflozin **EMPA-REG OUTCOME**[18] - Empagliflozin **EMPEROR-Reduced**[19] - Empagliflozin **EMPEROR-Preserved**[20] - Empagliflozin **VERTIS-CV**[21] - Ertugliflozin	Caution and review use with diuretics	**Precautions** very low carbohydrate intake, bowel preparation, perioperatively Reduced or insignificant glycaemic effectiveness at eGFR<45 ml/min/1.73m^2, however heart failure and chronic kidney disease benefits persist down to an eGFR<25 ml/min/1.73m^2. **Side effects** Dehydration, dizziness, genitourinary infections (advise adequate fluid intake and meticulous toileting hygiene), ketoacidosis, weight loss **Administration** Oral	Dapagliflozin and empagliflozin: PBS subsidised for use in combination with metformin, sulfonylurea or both. PBS subsidised for use with insulin **$$** Ertugliflozin: PBS subsidised for use in combination with metformin or sulfonylurea If on any SGLT2 i plus metformin, addition of either saxagliptin, sitagliptin or linagliptin (i.e. triple therapy) is PBS subsidised Not PBS subsidised for use as monotherapy or in combination with a thiazolidinedione (glitazone), or glucagon-like peptide-1
Glucagon-like peptide-1 (GLP-1) receptor agonists • dulaglutide • liraglutide • semaglutide	Stimulates beta-cell insulin release and slows gastric emptying Benefits include weight loss , BP lowering and very low risk of hypoglycaemia unless used with SU or insulin	**REWIND**[22] -Dulaglutide **LEADER**[23] -Liraglutide **SUSTAIN 6**[24] -Semaglutide **FLOW**[25] -Semaglutide	Avoid with history of pancreatitis or pancreatic malignancy	**Precautions** Dosage adjustment in moderate-severe renal impairment, Increased risk of pancreatitis **Side effects** Nausea, vomiting, weight loss, increased heart rate **Administration** Subcutaneous injection	Dulaglutide and semaglutide: PBS subsidised for use in combination with metformin, sulfonylurea or both **$$$** Dulaglutide and semaglutide: PBS subsidised for use with insulin PBS Authority required to initiate if SGLT2i did not achieve a clinically meaningful response, after which SGLT2i should be ceased. Not PBS subsidised for use as monotherapy or in combination with DPP-4 inhibitor (gliptin), a thiazolidinedione (glitazone) or an SGLT2 inhibitor
Insulin Can be prescribed as basal (eg glargine), prandial (eg aspart, glulisine) or premix/ coformulation (eg degludec/aspart)	Directly activates the insulin receptor	**UKPDS**[2] **ORIGIN**[26] - Insulin glargine **DEVOTE**[27] - Insulin degludec		**Precautions** Consider need for dosage adjustment in moderate-severe renal disease **Side effects** Hypoglycaemia, weight gain **Administration** Subcutaneous injection-consider early if BGL is very high	General schedule on PBS **$-$$$** Levemir Insulin: PBS subsidy restricted to Type 1 diabetes

† Gunton JE et.al. MJA 2014, 201(11), 650-53.

***COST: $ = $0-$499 $$ = $500-$999; $$$ = > $1,000 per annum cost to the PBS**

References:

1. UKPDS Group. Lancet 1998;352:854-65. **2.** UKPDS Group. Lancet 1998;352:837-53. **3.** ADVANCE Collaborative Group. NEJM 2008;358;2560-72. **4.** White WB, et al. NEJM 2013;369:1327-35. **5.** Zannad F,et al. Lancet 2015;385:2067-76. **6.** Scirica BM, et al. NEJM 2013;369:1317-26. **7.** Scirica BM, et al. Circulation 2014;130:1579-88. **8.** Green JB, Bethel MA, et al. NEJM 2015;373:232-42. **9.** Rosenstock J, et al. JAMA 2018; 321:69-79. **10.** Rosenstock J, et al. JAMA 2019; In Press. **11.** Meier JJ, et al. Diabetologia 2014;57:1320-1324. **12.** McGill JB, et al. Diabetes Care 2013;36:237- 44. **13.** Dormandy JA, et al. Lancet 2005;366:1279-89. **14.** Home PD, et al. Lancet 2009, 373:2125-35. **15.** Wiviott SD, et al. NEJM 2019; 380:347-357. **16.** McMurray JJV, et al. NEJM 2019;381:1995-2008. **17.** Heerspink HJL, et al. NEJM 2020;383:1436-1446. **18.** Zinman B, et al. NEJM 2015;372:2117-28. **19.** Packer M et al. NEJM 2020; 383:1413-24. **20.** Anker SD, et al. NEJM 2021; 385:1451-61. **21**. Cannon CP, et a. NEJM 2020; 383:1425-1435. **22.** Gerstein HC, et al. Lancet 2019; 394:121-130. **23.** Marso SP, et al. NEJM 2016;375:311-322. **24.** Marso SP, et al NEJM 2016;375: 1834-1844. **25.** Perkovic V et al. NEJM 2024;DOI: 10.1056/NEJMoa2403347 **26.** ORIGIN Trial Investigators, NEJM 2012, 367:319-328. **27.** Marso SP, et al. NEJM 2017; 377:723-732.