


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).

Effect of changes in therapy should be reviewed in 3 months.

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

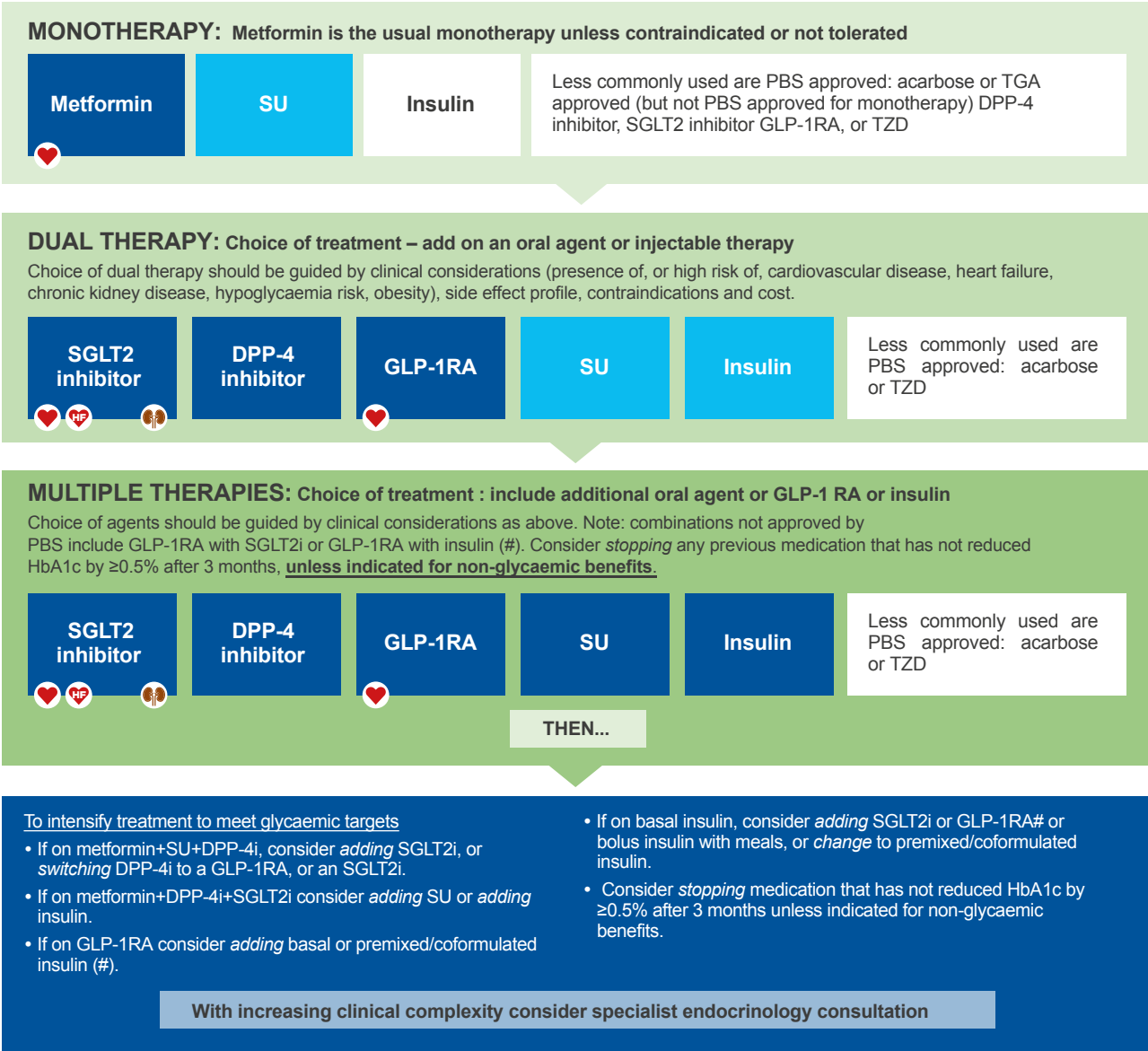
- Check patient understanding of self-management including drug treatment
- Ensure current therapies are clinically appropriate including comorbidities/therapies impacting glycaemic control
- Review medication adherence
- Assess tolerability, adverse effects and risk of interactions




+ Consider intensive weight management. Weight loss of $\geq 10\%$ may allow a reduction or cessation of glucose lowering medication. Options include:

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




 **Click here for the Australian Obesity Management Algorithm**

Review treatment in 3 months. **If HbA1c not at target:** Reinforce education regarding lifestyle measures, physical activity and weight control.



-  For patients with high risk/established CVD, studies have shown improved all cause and CV death and non-fatal MI when used with usual care.
-  For patients with high risk/established heart failure (HF)/HF hospitalisation, studies have shown improved outcomes when used with usual care.
-  For patients with CKD as defined by albuminuria and/or eGFR >30 ml/min/1.73m², studies have shown reductions in important major renal end points, when used with usual care.

Exenatide (Byetta) and dulaglutide (Trulicity) are the GLP-1RA approved on the PBS for use with insulin.

-  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.

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/m 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 - GliclazideMR	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) 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 Linagliptin, sitagliptin and vildagliptin are PBS subsidised for use with insulin	\$\$
Thiazolidinediones (TZD) • pioglitazone • rosiglitazone is no longer 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/m 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 • canagliflozin is no longer available in Australia	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	EMPA-REG OUTCOME ¹⁵ - Empagliflozin CANVAS ¹⁶ - Canagliflozin CREDESCENCE ¹⁷ - Canagliflozin DECLARE ¹⁸ - Dapagliflozin DAPA-HF ¹⁹ - Dapagliflozin EMPEROR-Reduced ²⁰ - Empagliflozin VERTIS-CV ²¹ - Ertugliflozin DAPA-CKD ²² - Dapagliflozin	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 SGLT2i 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 • exenatide • exenatide ER • liraglutide • lixisenatide • 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	ELIXA ^{23,24} -Lixisenatide LEADER ²⁵ -Liraglutide SUSTAIN 6 ²⁶ -Semaglutide EXSCEL ²⁷ -Exenatide REWIND ²⁸ - Dulaglutide	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	Exenatide, exenatide-ER, dulaglutide and semaglutide: PBS subsidised for use in combination with metformin, sulfonylurea or both Exenatide (but not exenatide ER) and dulaglutide: PBS subsidised for use with insulin 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, prandial or premix/coformulation	Directly activates the insulin receptor	UKPDS ² ORIGIN ²⁹ - Insulin glargine DEVOTE ³⁰ - 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.

References:

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