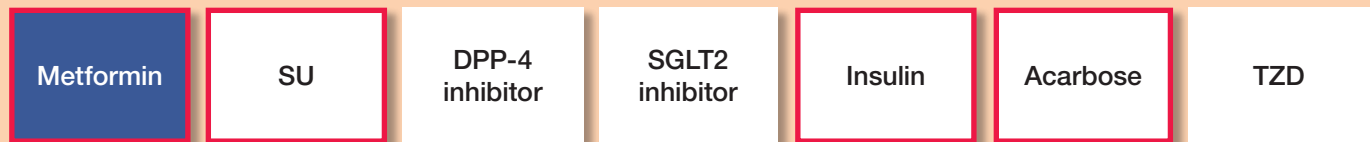


AUSTRALIAN BLOOD GLUCOSE TREATMENT ALGORITHM FOR TYPE 2 DIABETES

All patients should receive education regarding lifestyle measures: healthy diet, physical activity and weight control
 Determine the individual's HbA_{1c} target – this will commonly be ≤ 53 mmol/mol (7.0%).
 If not at target, or if an HbA_{1c} reduction of ≥ 0.5% is not achieved after 3 months, move down the algorithm.

First line: Metformin is the usual first-line therapy unless contraindicated or not tolerated



If HbA_{1c} target not achieved in 3 months:

- check and review current therapies, stop any that fail to improve glycaemic control
- check patient understanding and self-management
- review use of therapies
- exclude other comorbidities/therapies impacting on glycaemic control
- reinforce lifestyle measures

Second line: If metformin was not used first line, add it now, if not contraindicated

Sulfonylureas (SU) are the usual initial agent to add to metformin. If SU are contraindicated or not tolerated, another agent may be used.



If HbA_{1c} target not achieved in 3 months:

- check and review current therapies, stop any that fail to improve glycaemic control
- check patient understanding and self-management
- review use of therapies
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- reinforce lifestyle measures

Third line: Consider triple oral therapy or addition of GLP-1RA or insulin

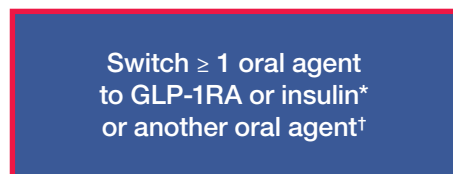


If HbA_{1c} target not achieved in 3 months:

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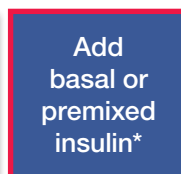
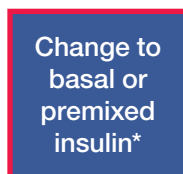
THEN

If on triple oral therapy



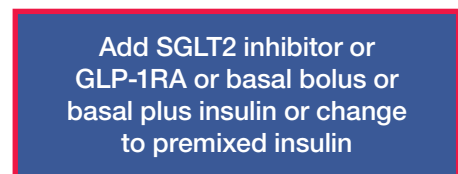
OR

If on GLP-1RA



OR

If on basal insulin*



PBS = Pharmaceutical Benefits Scheme, SU=sulfonylurea, TZD= thiazolidinedione, DPP-4 = dipeptidyl peptidase-4, GLP-1RA= glucagon like peptide 1 receptor agonist, SGLT2 = sodium glucose transporter.

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). White boxes indicate alternate approaches (order is not meant to denote any specific preference). Red outlines indicate the classes of glucose lowering agent that include PBS subsidised products.

* Unless metformin is contraindicated, or not tolerated, it is often therapeutically useful to continue it in combination with insulin in people with Type 2 diabetes.

† Switching an oral agent is likely to have the smallest impact on glycaemia.

AUSTRALIAN BLOOD GLUCOSE TREATMENT ALGORITHM FOR TYPE 2 DIABETES

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 <ul style="list-style-type: none"> 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 administration Start at low dose and up-titrate Slow release preparations available	General schedule on PBS
Sulfonylureas <ul style="list-style-type: none"> 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 administration Start at low dose and up-titrate Slow release preparation available	General schedule on PBS
Dipeptidyl peptidase-4 (DPP-4) inhibitors <ul style="list-style-type: none"> 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	Pancreatitis ⁹	Precautions Nasopharyngitis-often subsides in 10-14 days Side Effects Rash, pancreatitis, GI disturbances, weight neutral Administration Oral administration Dosage adjustment in renal impairment (except Linagliptin) ¹⁰	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) Linagliptin and Sitagliptin are PBS subsidised for use with insulin
Thiazolidinediones (TZD) <ul style="list-style-type: none"> pioglitazone rosiglitazone 	Transcription factor peroxisome proliferator-activated receptor PPAR γ agonists Lowers glucose levels through insulin sensitisation	PROACTIVE ¹¹ - Pioglitazone RECORD ¹² - 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 administration	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 <ul style="list-style-type: none"> 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 administration Take with meals as tolerated	General schedule on PBS
Sodium-glucose co-transporter-2 (SGLT2) inhibitors <ul style="list-style-type: none"> canagliflozin dapagliflozin empagliflozin 	Inhibits a Sodium-glucose cotransporter to induce urinary glucose loss and decrease blood glucose levels	EMPA-REG OUTCOME ¹³ - Empagliflozin	Diminished efficacy with renal impairment (eGFR < 60 ml/min/m ²)	Precautions Avoid use with loop diuretics Side effects Dehydration, dizziness, genitourinary infections (advise adequate fluid intake and meticulous toileting hygiene), ketoacidosis, weight loss Administration Oral administration	Dapagliflozin and Empagliflozin: PBS subsidised for use in combination with Metformin, Sulfonylurea or both PBS subsidised for use with insulin Not PBS subsidised for use as monotherapy or in combination with a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin) or a glucagon-like peptide-1 Canagliflozin: PBS subsidisation withdrawn
Glucagon-like peptide-1 (GLP-1) receptor agonists <ul style="list-style-type: none"> exenatide exenatide ER liraglutide lixisenatide 	Stimulates beta-cell insulin release and slows gastric emptying	ELIXA ^{14,15} - Lixisenatide LEADER ¹⁶ - Liraglutide	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 Administration Subcutaneous injection	Exenatide and Exenatide ER: PBS subsidised for use in combination with Metformin, Sulfonylurea or both Exenatide: PBS subsidised for use with insulin Not PBS subsidised for use as monotherapy or in combination with dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone) or a SGLT2 inhibitor
Insulin	Directly activates the insulin receptor.	UKPDS ² ORIGIN ¹⁷ - Insulin Glargine		Precautions Consider need for dosage adjustment in moderate-severe renal disease Side effects Hypoglycaemia, weight gain Administration Subcutaneous injection Considered early if BGL is very high	General schedule on PBS Levemir Insulin: PBS subsidisation restricted to Type 1 diabetes

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

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