MANAGEMENT ALGORITHM

**AUSTRALIAN TYPE 2 DIABETES**

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

Determine the individual’s HbA1c target – commonly ≤3 mmol/mol (7.0%) but should be reviewed regularly.

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

Move down the algorithm if not at target HbA1c:
- Check and review current therapies
- Review adherence to medications
- Check for side effects
- Exclude other comorbidities/therapies impacting on glycaemic control
- Check patient understanding of treatment and self-management.

**FIRST LINE:** Metformin is usual first line therapy unless contraindicated or not tolerated
- Metformin
- SU
- Insulin
- Check HbA1c target in 3 months: If not achieved move down algorithm

**SECOND LINE:** Choice of treatment – add on an oral agent or injectable therapy
Choice of second line agent should be guided by clinical considerations (presence of, or high risk of cardiovascular disease, heart failure, chronic kidney disease, hypoglycaemia), side effect profile, contraindications and cost.

- SGLT2 inhibitor
- DPP-4 inhibitor
- SU
- GLP-1RA
- Insulin
- Less commonly used are PBS approved acarbose or TGA approved DPP-4 inhibitor, SGLT2 inhibitor or TZD

**THIRD LINE:** Choice of treatment: include additional oral agent or GLP-1 RA or insulin
Choice of third-line agent should be guided by clinical considerations as above. Note: combinations not approved by PBS include GLP-1RA with SGLT2i or GLP-1RA with insulin (#). Consider stopping any second-line medication that has not reduced HbA1c by ≥0.5% after 3 months unless indicated for non-glycaemic benefits.

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- DPP-4 inhibitor
- SU
- GLP-1RA
- Insulin
- Less commonly used are PBS approved acarbose or TZD

**With increasing clinical complexity consider specialist endocrinology consultation**

- 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.
- White boxes indicate less commonly used approaches.

**PBS** = Pharmaceutical Benefits Scheme, **MACE** = major adverse cardiovascular events, **MREP** = major renal end points, **HF** = heart failure, **CKD** = chronic kidney disease, **SU** = sulfonylureas, **TZD** = thiazolidinedione, **DPP-4i** = dipeptidyl peptidase-4 inhibitor, **GLP-1RA** = glucagon like peptide-1 receptor agonist, **SGLT2i** = sodium glucose co-transporter inhibitor.

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

\[\text{Visit diabetesaustralia for more information.}\]
<table>
<thead>
<tr>
<th>Glucose-lowering Class and Drugs</th>
<th>Mechanism of Action</th>
<th>Outcome data</th>
<th>Contraindications</th>
<th>Precautions, Side Effects and Administration</th>
<th>Cost and Accessibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanide</td>
<td>Metformin</td>
<td>Reduces hepatic glucose output, lowers fasting glucose levels</td>
<td>UKPD06</td>
<td>Renal impairment (eGFR &lt;30 ml/min/1.73 m²)</td>
<td>Precautions: Suspect treatment during acute disease/conditions with the potential to cause tissue hypoxia or alter renal function. Side Effects: G1 side effects, lactic acidosis, weight neutral. Administration: Oral. Start at low dose and up-titrte. Slow release preparations available.</td>
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<tr>
<td>Sulfonylureas</td>
<td>Gliclazide</td>
<td>Triggers insulin release in a glucose-independent manner</td>
<td>UKPD05 ADVANCE3</td>
<td>Severe renal or hepatic impairment</td>
<td>Precautions: Hypoglycaemia. Side Effects: Weight gain. Administration: Oral. Start at low dose and up-titrte. Slow release preparations available.</td>
</tr>
<tr>
<td>Dipeptidylpeptidase-4 (DPP-4) inhibitors</td>
<td>Alogliptin</td>
<td>Decreases inactivation of glucagon-like peptide (GLP)-1 thereby increasing its effects on GLP-1-stimulated beta cell insulin release</td>
<td>EXAMINE14 Aalogliptin SAVOR-TIMI 53A1 Saxagliptin TECOS3 Sitagliptin CARAMELINA4 Linagliptin CAROLINA5 Linagliptin vs Glimepiride</td>
<td>Pancreatitis or Hospitalisation due to heart failure with saxagliptin6</td>
<td>Precautions: Nasopharyngitis offtendsubside in 10-14 days. Side Effects: Rash, pancreatitis, GL disturbances, weight neutral. Administration: Oral. Dosage adjustment in renal impairment (except linagliptin)7.</td>
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<tr>
<td>Thiazolidinediones (TZD)</td>
<td>Pioglitazone</td>
<td>Transcription factor peroxisome proliferator-activated receptor-PPARγ agonists. Lowers glucose levels through insulin sensitization</td>
<td>PROACTIVE13 Pioglitazone RECORD4 Rosiglitazone</td>
<td></td>
<td>Precautions: Symptomatic heart failure. Side Effects: Fluid retention, heart failure, increased risk of non-avai fractures in women, increased risk of bladder cancer, weight gain. Administration: Oral.</td>
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<tr>
<td>Alpha 1 glucosidase inhibitors</td>
<td>Acarbose</td>
<td>Slows intestinal carbohydrate absorption and reduces Postprandial glucose levels</td>
<td></td>
<td>Severe renal impairment (creatinine clearance &lt;25 ml/min/1.73 m²)</td>
<td>Precautions: Gastrintestinal disorders associated with malabsorption. Side effects: Bloating and flatulence, weight neutral. Administration: Oral. Take with meals as tolerated.</td>
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<tr>
<td>Sodium-glucose co-transporter-2 (SGLT2) inhibitors</td>
<td>Dapagliflozin</td>
<td>Inhibits a Sodium-glucose co-transporter to reduce urinary glucose loss and decrease blood glucose levels</td>
<td>EMPA-REG OUTCOME3 - Empagliflozin CANVAS3 - Canagliflozin CREDENCE4 - Canagliflozin DECLARE5 - Dapagliflozin DAPA-HF6 - Dapagliflozin EMPEROR-Reduced8 Empagliflozin</td>
<td>Contraindicated at eGFR &lt;45 ml/min/1.73 m²</td>
<td>Avoid use with loop diuretics.</td>
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<tr>
<td>Insulin</td>
<td>Directly activates the insulin receptor</td>
<td></td>
<td>UKPD05 ORIGIN2 Insulin glargine DEVOTE3 Insulin degludec</td>
<td></td>
<td>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.</td>
</tr>
</tbody>
</table>

1 Glenton JE et al. MJA 2014, 201(11), 650-53.

References: