Please Note: This algorithm is not intended for treatment and target selection in children or in women who are or could become pregnant.

Step 1: Determine Individualized Glycemic Target
A1C Target Range: Select based on age, duration of diabetes, patient preference, comorbidities, hypoglycemia risk, and other factors.

<table>
<thead>
<tr>
<th>Major Comorbidity</th>
<th>Absent or Mild</th>
<th>Moderate</th>
<th>Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent (and/or &gt;10-15 years of life expectancy)</td>
<td>6.0-7.0%</td>
<td>7.0-8.0%</td>
<td>7.5-8.5%</td>
</tr>
<tr>
<td>Present (and/or 5-10 years of life expectancy)</td>
<td>7.0-8.0%</td>
<td>7.5-8.5%</td>
<td>7.5-8.5%</td>
</tr>
<tr>
<td>Marked (and/or &lt;5 years of life expectancy)</td>
<td>8.0-9.0%</td>
<td>8.0-9.0%</td>
<td>8.0-9.0%</td>
</tr>
</tbody>
</table>

Microvascular complications include stroke, retinopathy, nephropathy, or neuropathy.

Step 2: Initiate Medication Therapy
If significant weight loss or ketonuria, use insulin (hospitalize if acidic). Otherwise:
- Start metformin if A1C above patient's target but <9%.
- Start metformin and a second medication if A1C ≥9% (see Step 3).

Step 3: If A1C above patient's target range, increase dosage(s) and/or add another medication
Select additional medication(s) based on formulary options, side effects, comorbidities, cost, medication regimen complexity, and patient preference.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Weight</th>
<th>A1C</th>
<th>Risk of Hypoglycemia</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>↓↓</td>
<td>↓</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>DPP-4 Inhibitor</td>
<td>-</td>
<td>↓</td>
<td>-</td>
<td>↑↑</td>
</tr>
<tr>
<td>GLP-1 Receptor Agonist</td>
<td>↓↓</td>
<td>↓</td>
<td>-</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Insulin</td>
<td>↑↑/↑↑</td>
<td>↓↓</td>
<td>↑↑</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>SGLT2 Inhibitor</td>
<td>-/↓</td>
<td>↓</td>
<td>-</td>
<td>↑↑</td>
</tr>
<tr>
<td>Sulfonyurea</td>
<td>↑↑</td>
<td>↓↓</td>
<td>↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>Thiazolidinedione</td>
<td>↑</td>
<td>↓↓</td>
<td>-</td>
<td>↑↑</td>
</tr>
</tbody>
</table>

Do not use GLP-1 Receptor Agonists and DPP-4 inhibitors together as no A1C benefit.

Metformin
- Start 500mg daily with meals and increase no faster than 500mg/day each week.
- If GI symptoms occur, may increase more slowly.
- Max dose: Regular release tablets: 2,550mg divided BID or TID.
- XR tablets: 2,000mg daily or divided BID.
- Monitor and supplement vitamin B12 as needed with long term use.
- Discontinue if eGFR <30mL/min/1.73m².
- Warning: May cause lactic acidosis.

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors
- Saxagliptin (Onglyza®) Dose: 2.5-5mg daily. Use 2.5mg if eGFR ≤50mL/min/1.73m².
- May increase risk of heart failure, especially in patients with heart or kidney disease.
- Linagliptin (Tradjenta®) 5mg daily.
- Sitagliptin (Januvia®) 100mg daily (reduce dose if eGFR ≤50mL/min/1.73m²).

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists
- Exenatide (Byetta®) Start 5mcg BID SC in thigh, abdomen, or upper arm.
- May increase to 10mcg BID after 1 month. Administer within 60 minutes before meals.
- Exenatide ER (Bydureon®) Start 2mg SC weekly.
- For Exenatide/Exenatide ER: See prescribing reference when eGFR <60mL/min/1.73m².
- Liraglutide (Victoza®) Start 0.6mg SC daily in thigh, abdomen, or upper arm.
- Increase to 1.2mg daily in 1 week. May increase to 1.8mg daily.
- Pancreatitis and acute kidney injury have been reported.GI side effects common.
- Warning: May increase risk of thyroid tumor.

Insulin - See Insulin algorithm.

Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors
- Canagliflozin (Invokana®) Start 100mg daily before first meal. May increase to 300mg daily.
- Dapagliiflozin (Farxiga®) Start 5mg every day. May increase to 10mg daily.
- Empagliflozin (Jardiance®) Start 10mg daily. May increase to 25mg daily.
- May cause volume depletion, orthostatic hypotension, genital fungal infections, and UTI.
- For all SGLT2 Inhibitors: See prescribing reference when eGFR <60mL/min/1.73m².

Sulfonyureas
- Glipizide Start 2.5-5mg daily - max 20mg BID. ER formulation dosed 5-20mg daily.
- Glimepiride Start 1-2mg daily - max 8mg daily.
- May cause hypoglycemia, weight gain.

Thiazolidinedione (TZD)
- Pioglitazone (Actos®) Start 15mg daily; may increase to 30-45mg daily.
- May cause hypoglycemia, weight gain.

Medications on the IHS National Core Formulary are in BOLD above.

This is a summary of the most commonly ordered non-insulin diabetes medications and drug classes from the IHS National Supply Service Center. No endorsement of specific products is implied. Please consult a complete prescribing reference for more detailed information.