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 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>

Major comorbidity includes but is not limited to significant CVD; recent stroke; life-threatening malignancy; or severe CKD, COPD, or chronic liver disease. Microvascular disease: retinopathy, neuropathy, or CKD.

Adapted from the VA/DoD Management of Diabetes Mellitus Guideline

**Step 2: Initiate Medication Therapy**
If A1C not within individualized target range
If significant weight loss or ketonuria, use insulin (hospitalize if acidicotic). 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: Increase Dosage(s) and/or Add Another Medication**
Select additional medication(s) based on formulary options, side effects, cost, comorbidities (e.g., CVD), 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>- to ↓</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>↑↑ to ↑↑↑</td>
<td>↓↓↓</td>
<td>↑↑↑</td>
<td>$$ to $$$</td>
</tr>
<tr>
<td>SGLT2 Inhibitor</td>
<td>↓</td>
<td>↓</td>
<td>-</td>
<td>$$</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td>↑↑</td>
<td>↓</td>
<td>↑</td>
<td>$</td>
</tr>
<tr>
<td>Thiazolidinedione (TZD)</td>
<td>↑</td>
<td>↓↓</td>
<td>-</td>
<td>$</td>
</tr>
</tbody>
</table>

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

**Metformin**
Monitor and supplement vitamin B12 as needed with long term use. Discontinue if eGFR <30mL/min/1.73m².
Warning: May cause lactic acidosis (rare). 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.

**Dipeptidyl Peptidase-4 (DPP-4) Inhibitors**
- Alogliptin (Nesina®) Start 25mg daily. May increase risk of heart failure.
- Sitagliptin (Januvia®) Start 100mg daily.
- Linagliptin (Tradjenta®) Start 5mg daily.
- Saxagliptin (Onglyza®) Start 2.5-5mg daily. May increase risk of heart failure.

**Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists**
GL side effects common.
Warning: May increase risk of thyroid tumor.
Dulaglutide (Trulicity®) Start 0.75mg SC weekly. May increase to 1.5mg/week.
Exenatide ER (Bydureon®) Start 2mg SC weekly.*
Liraglutide (Victoza®) Start 0.6mg SC daily. Increase to 1.2mg daily in 1 week. May increase to 1.8mg daily. *Indicated to reduce the risk of CV events in patients with established CVD.
Semaglutide (Ozempic®) Start 0.25mg SC weekly for 4 weeks, then increase to 0.5mg weekly for 4 weeks. May increase to 1mg weekly.

**Insulin** - See Insulin Therapy Algorithm.

**Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors**
May cause volume depletion, orthostatic hypotension, genital fungal infections, DKA, acute kidney injury, and UTI.
Canagliflozin (Invokana®) Start 100mg daily before first meal. May increase to 300mg daily.
Warning: May increase risk of lower limb amputations. *Indicated to reduce the risk of CV events in patients with established CVD.
Empagliflozin (Jardiance®) Start 10mg daily. May increase to 25mg daily. *Indicated to reduce the risk of CV death in patients with established CVD.

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

**Thiazolidinedione (TZD)**
May increase risk of bone fracture. Do not use in patients with bladder cancer. Check LFTs before starting. May cause weight gain.
Warning: Increased risk of heart failure.

**Pioglitazone (Actos®)** Start 15mg daily; may increase to 30-45mg daily. Max A1C changes may take up to 12 weeks to occur.
*See prescribing reference when eGFR <60mL/min/1.73m².*

Medications on the IHS National Core Formulary are in **BOLD** above.
Please consult a complete prescribing reference for more detailed information. 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.

Last updated March 2019