A1C 6.5 – 7.5%**

- Monotherapy
  - MET + TZD 2
  - DPP4 1
  - AGI 3

- Dual Therapy
  - MET + GLP-1 or DPP4 1, or TZD 2
  - SU or Glinide 4,5

- Triple Therapy
  - MET + GLP-1 or DPP4 1, or TZD 2
  - GLP-1 or DPP4 1, or SU 7

A1C 7.6 – 9.0%

- Dual Therapy 8
  - MET + GLP-1 or DPP4 1, or TZD 2
  - SU or Glinide 4,5

A1C > 9.0%

- Under Treatment
  - INSULIN ± Other Agent(s) 6

- Symptoms
  - INSULIN ± Other Agent(s) 6

- Drug Naive
  - INSULIN ± Other Agent(s) 6

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AACE/ACE Algorithm for Glycemic Control Subcommittee

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- May not be appropriate for all patients
- For patients with diabetes and A1c < 6.5%, pharmacologic Rx may be considered
- If A1c goal not achieved safely
- DPP4 if ↑ PPG and ↑ FPG or GLP-1 if ↑ PPG
- Insulin if metabolic syndrome and/or nonalcoholic fatty liver disease (NAFLD)
- AGI if ↓ PPG
- Glinide if ↑ PPG or SU if ↑ FPG
- Low-dose secretagogue recommended
  - a) Discontinue insulin secretagogue with multidose insulin
  - b) Can use pramlintide with prandial insulin
- Decrease secretagogue by 50% when added to GLP-1 or DPP-4
- If A1C < 8.5%, combination Rx with agents that cause hypoglycemia should be used with caution
- If A1C > 8.5%, in patients on Dual Therapy, insulin should be considered
- GLP-1 not approved for initial combination Rx

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**Table 1**

**Summary of Key Benefits and Risks of Medications**

Benefits are classified according to major effects on fasting glucose, postprandial glucose, and nonalcoholic fatty liver disease (NAFLD). Eight broad categories of risks are summarized. The intensity of the background shading of the cells reflects relative importance of the benefit or risk.*

<table>
<thead>
<tr>
<th>MEDICATIONS*</th>
<th>Metformin (MET)</th>
<th>DPP4 Inhibitor</th>
<th>GLP-1 Agonist (Incretin Mimetic)</th>
<th>Sulfonylurea (SU)</th>
<th>Thiazolidinedione (TZD)</th>
<th>Colesevelam</th>
<th>Alpha-glucosidase inhibitor (AGI)</th>
<th>Insulin</th>
<th>Pramlintide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postprandial Glucose (PPG) - lowering</td>
<td>Mild</td>
<td>Moderate</td>
<td>Moderate to Marked</td>
<td>Moderate</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate to Marked</td>
<td>Moderate to Marked</td>
<td>Moderate to Marked</td>
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<tr>
<td>Fasting glucose (FPG) - lowering</td>
<td>Moderate</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mild</td>
<td>Neutral</td>
<td>Mild</td>
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<tr>
<td>Nonalcoholic fatty liver disease (NAFLD)</td>
<td>Mild</td>
<td>Neutral</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
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<td>Risks</td>
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<td></td>
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<td></td>
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<tr>
<td>Hypoglycemia</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate to Severe</td>
<td>Neutral</td>
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<td>Gastrointestinal Symptoms</td>
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<td>Neutral</td>
<td>Moderate</td>
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<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td>Risk of use with renal insufficiency</td>
<td>Severe</td>
<td>Reduce Dosage</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Mild</td>
<td>Neutral</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Contraindicated in Liver Failure or Predisposition to Lactic Acidosis</td>
<td>Severe</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td>Heart failure / Edema</td>
<td>Contraindicated in CHF</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Mild / Moderate</td>
<td>Neutral unless with TZD</td>
<td>Neutral</td>
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<tr>
<td>Weight Gain</td>
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<td>Benefit</td>
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<td>Neutral</td>
<td>Mild to Moderate</td>
<td>Benefit</td>
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<tr>
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<td>Moderate</td>
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<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
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</tr>
</tbody>
</table>

* The abbreviations used here correspond to those used on the algorithm, (Fig. 1).
** The term ‘glinide’ includes both repaglinide and nateglinide.