AACE/ACE COMPREHENSIVE DIABETES MANAGEMENT ALGORITHM 2015

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Complications-Centric Model for Care of the Overweight/Obese Patient

**STEP 1**
EVALUATION FOR COMPLICATIONS AND STAGING

**CARDIOMETABOLIC DISEASE**
- NO COMPLICATIONS
  - BMI 25–26.9, or BMI ≥ 27

**BIOMECHANICAL COMPLICATIONS**
- BMI ≥ 27 WITH COMPLICATIONS
  - Stage Severity of Complications
    - LOW
    - MEDIUM
    - HIGH

**STEP 2**
SELECT:

- Therapeutic targets for improvement in complications
- Treatment modality
- Treatment intensity for weight loss based on staging

**Lifestyle Modification:**
- MD/RD counseling; web/remote program; structured multidisciplinary program

**Medical Therapy:**
- Phentermine; orlistat; lorcaserin; phentermine/topiramate ER;
  - naltrexone/bupropion; liraglutide

**Surgical Therapy (BMI ≥ 35):**
- Lap band; gastric sleeve; gastric bypass

**STEP 3**
If therapeutic targets for improvements in complications not met, intensify lifestyle and/or medical and/or surgical treatment modalities for greater weight loss
INDIVIDUALIZE GOALS

**A1c ≤ 6.5%**
For patients without concurrent serious illness and at low hypoglycemic risk

**A1c > 6.5%**
For patients with concurrent serious illness and at risk for hypoglycemia
**Glycemic Control Algorithm**

**LIFESTYLE MODIFICATION**

(Including Medically Assisted Weight Loss)

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**MONOTHERAPY**

- Metformin
- GLP-1 RA
- SGLT-2i
- DPP-4i
- AGI
- TZD
- SU/GLN

**DUAL THERAPY**

- GLP-1 RA
- SGLT-2i
- DPP-4i
- TZD
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGI
- SU/GLN

**TRIPLE THERAPY**

- GLP-1 RA
- SGLT-2i
- TZD
- Basal Insulin
- DPP-4i
- Colesevelam
- Bromocriptine QR
- AGI
- SU/GLN

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**ENTRY A1c < 7.5%**

**ENTRY A1c ≥ 7.5%**

**ENTRY A1c > 9.0%**

**SYMPTOMS**

- **NO**
  - DUAL Therapy
  - OR
  - TRIPLE Therapy
- **YES**
  - INSULIN ± Other Agents

**ADD OR INTENSIFY INSULIN**

- Refer to Insulin Algorithm

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**PROGRESSION OF DISEASE**

*Order of medications listed represents a suggested hierarchy of usage*

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**LEGEND**

- ✔ Few adverse events or possible benefits
- ⚠️ Use with caution

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START BASAL (long-acting insulin)

- **A1c < 8%**
  - TDD: 0.1–0.2 U/kg
  - Insulin titration every 2–3 days to reach glycemic goal:
    - Fixed regimen: Increase TDD by 2 U
    - Adjustable regimen:
      - FBG > 180 mg/dL: add 20% of TDD
      - FBG 140–180 mg/dL: add 10% of TDD
      - FBG 110–139 mg/dL: add 1 Unit
    - If hypoglycemia, reduce TDD by:
      - BG < 70 mg/dL: 10% – 20%
      - BG < 40 mg/dL: 20% – 40%

- **A1c > 8%**
  - TDD: 0.2–0.3 U/kg

Consider discontinuing or reducing sulfonylurea after basal insulin started (basal analogs preferred to NPH)

**Glycemic Goal:**
- <7% for most patients with T2DM; fasting and premeal BG < 110 mg/dL; absence of hypoglycemia
- A1c and FBG targets may be adjusted based on patient’s age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk

INTENSIFY (prandial control)

- Add GLP-1 RA or SGLT-2i or DPP-4i
- TDD: 0.3–0.5 U/kg
  - 50% Basal Analog
  - 50% Prandial Analog
  - Less desirable: NPH and regular insulin or premixed insulin

- Add Prandial Insulin
  - Increase prandial dose by 10% for any meal if the 2-hr postprandial or next premeal glucose is > 180 mg/dL
  - Premixed: Increase TDD by 10% if fasting/premeal BG > 180 mg/dL
  - If fasting AM hypoglycemia, reduce basal insulin
  - If nighttime hypoglycemia, reduce basal and/or pre-supper or pre-evening snack short/rapid-acting insulin
  - If between-meal daytime hypoglycemia, reduce previous premeal short/rapid-acting insulin
**Dyslipidemia**

**Lipid Panel: Assess CVD Risk**

**Statin Therapy**
- If statin-intolerant
  - Try alternate statin, lower statin dose or frequency, or add nonstatin LDL-C-lowering therapies

**IF TG > 500 mg/dL**, fibrates, omega-3 ethyl esters, niacin

**Repeat lipid panel: assess adequacy, tolerance of therapy**

**Intensify therapies to attain goals according to risk levels**

**Risk Levels**

<table>
<thead>
<tr>
<th></th>
<th><strong>Desirable Levels</strong></th>
<th><strong>Desirable Levels</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C  (mg/dL)</td>
<td>&lt;100</td>
<td>&lt;70</td>
</tr>
<tr>
<td>Non-HDL-C (mg/dL)</td>
<td>&lt;130</td>
<td>&lt;100</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>&lt;150</td>
<td>&lt;150</td>
</tr>
<tr>
<td>TC/HDL-C</td>
<td>&lt;3.5</td>
<td>&lt;3.0</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>&lt;90</td>
<td>&lt;80</td>
</tr>
<tr>
<td>LDL-P (nmol/L)</td>
<td>&lt;1200</td>
<td>&lt;1000</td>
</tr>
</tbody>
</table>

**If Not at Desirable Levels:**
- Intensify TLC (weight loss, physical activity, dietary changes) and glycemic control; Consider additional therapy

**To Lower LDL-C:**
- Intensify statin, add ezetimibe &/or colesvelem &/or niacin

**To Lower Non-HDL-C, TG:**
- Intensify statin &/or add OM3EE &/or fibrates &/or niacin

**To Lower Apo B, LDL-P:**
- Intensify statin &/or ezetimibe &/or colesvelem &/or niacin

Assess adequacy & tolerance of therapy with focused laboratory evaluations and patient follow-up

*EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED

**Hypertension**

**Goal:** Systolic ~130, Diastolic ~80 mm Hg

For initial blood pressure >150/100 mm Hg: Dual Therapy

<table>
<thead>
<tr>
<th></th>
<th>Thiazide</th>
<th>Calcium Channel Blocker</th>
<th>β-blocker</th>
</tr>
</thead>
</table>

If not at goal (2–3 months)
- Add β-blocker or calcium channel blocker or thiazide diuretic

If not at goal (2–3 months)
- Add next agent from the above group, repeat

If not at goal (2–3 months)
- Additional choices (α-blockers, central agents, vasodilators, spironolactone)

Achievement of target blood pressure is critical
# Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>GLP-1 RA</th>
<th>SGLT-2i</th>
<th>DPP-4i</th>
<th>AGi</th>
<th>TZD</th>
<th>SU</th>
<th>GLN</th>
<th>COLSVL</th>
<th>BCR-QR</th>
<th>INSULIN</th>
<th>PRAML</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HYPO</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate to Severe</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>WEIGHT</strong></td>
<td>Slight Loss</td>
<td>Loss</td>
<td>Loss</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Loss</td>
</tr>
<tr>
<td><strong>RENAL/GU</strong></td>
<td>Contraindicated CKD Stage 3B,4,5</td>
<td>Exenatide Contraindicated CrCl &lt; 30</td>
<td>Genital Mycotic Infections</td>
<td>Dose Adjustment May be Necessary (Except Linagliptin)</td>
<td>Neutral</td>
<td>May Worsen Fluid Retention</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk &amp; Fluid Retention</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td><strong>GI Sx</strong></td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>CVD</strong></td>
<td>Benefit</td>
<td>Neutral</td>
<td>Increased LDL</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Safe</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>BONE</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate Bone Loss</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
</tbody>
</table>

- **Neutral**: Few adverse events or possible benefits
- **Yellow**: Use with caution
- **Orange**: Likelihood of adverse effects

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1) Lifestyle optimization and education are essential for all patients with diabetes. Lifestyle modification designed for weight loss, including medical and surgical interventions approved for the treatment of obesity, should be considered as primary approaches for therapeutic benefits in overweight and obese patients with diabetes, and for prevention of diabetes in high risk patients with prediabetes. The treatment of overweight/obesity in patients with type 2 diabetes and prediabetes should proceed according to the Obesity Treatment Algorithm. Effective interventions for weight loss involve a multidisciplinary team. The need for medical therapy for weight loss or glycemic control should not be considered as a failure of lifestyle management, but as an adjunct to it.

2) The A1c target must be individualized, based on numerous factors, such as age, comorbid conditions, duration of diabetes, risk of hypoglycemia, patient motivation, adherence, life expectancy, etc. An A1c of 6.5% or less is still considered optimal if it can be achieved in a safe and affordable manner, but higher targets may be appropriate and may change in a given individual over time.

3) Minimizing risk of hypoglycemia is a priority. It is a matter of safety, adherence, and cost.

4) Minimizing risk of weight gain is a priority. It too is a matter of safety, adherence, and cost.

5) Glycemic control targets include fasting and postprandial glucose as determined by self blood glucose monitoring.

6) The choice of therapies must be individualized based on attributes of the patient (as above) and the medications themselves (see Profiles of Antidiabetic Medications). Attributes of medications that affect their choice include: risk of inducing hypoglycemia, risk of weight gain, ease of use, cost, and safety impact of kidney, heart, or liver disease. This algorithm includes every FDA-approved class of medications for diabetes. This algorithm also stratifies choice of therapies based on initial A1c.

7) The algorithm provides guidance to what therapies to initiate and add, but respects individual circumstances that would make different choices.

8) Therapies with complementary mechanisms of action must typically be used in combinations for optimum glycemic control.

9) Effectiveness of therapy must be evaluated frequently until stable (e.g. every 3 months) using multiple criteria including A1c, SMBG records including both fasting and postprandial data, documented and suspected hypoglycemia, and monitoring for other potential adverse events (weight gain, fluid retention, hepatic, renal, or cardiac disease), and monitoring of comorbidities, relevant laboratory data, concomitant drug administration, diabetic complications, and psycho-social factors affecting patient care.

10) Safety and efficacy should be given higher priorities than initial acquisition cost of medications per se since cost of medications is only a small part of the total cost of care of diabetes. In determining the cost of a medication, consideration should be given to monitoring requirements, risk of hypoglycemia and weight gain, etc.

11) The algorithm should be as simple as possible to gain physician acceptance and improve its utility and usability in clinical practice.

12) The algorithm should serve to help educate the clinician as well as to guide therapy at the point of care.

13) The algorithm should conform, as nearly as possible, to a consensus for current standard of practice of care by expert endocrinologists who specialize in the management of patients with type 2 diabetes and have the broadest experience in outpatient clinical practice.

14) The algorithm should be as specific as possible, and provide guidance to the physician with prioritization and a rationale for selection of any particular regimen.

15) Rapid-acting insulin analogs are superior to Regular because they are more predictable.

16) Long-acting insulin analogs are superior to NPH insulin because they provide a fairly flat response for approximately 24 hours and provide better reproducibility and consistency both between subjects and within subjects, with a corresponding reduction in the risk of hypoglycemia.

This document represents the official position of the American Association of Clinical Endocrinologists and the American College of Endocrinology. Where there were no RCTs or specific FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Many details that could not be included in the graphic summary (Figure) are described in the text.

All necessary author disclosures are made to AACE and are on file at the main office. Please contact Lori Clawges at AACE for further inquiries.