November 2019

Pharmacy Pearls

Best Practices for Management of Type 2 Diabetes

The CDC estimates that 43.3% of the US population has prediabetes or diabetes. Diabetes was the seventh leading cause of death in the U.S. in 2015 and the total direct and indirect costs of diagnosed diabetes in 2012 was $245 billion. Given the indisputable negative effects on health care costs, morbidity, and mortality; optimizing diabetes control in our population is vital.

Along with the recently released 2019 ADA Standards of Care in Diabetes and MCMS Diabetes Guidelines, AHP is endorses the following principles for Type 2 diabetes management:

1. **Optimize metformin therapy:** *Click here for details*
   - Preferred first-line agent due to efficacy, safety, tolerability, cost, and clinical experience
   - Maximize dose (max: 2500 mg/day); use the highest dose tolerable rather than stopping
   - Should not be discontinued when other agents are added (including insulin) because clinical benefit remains and hypoglycemia risk is low
   - GI intolerance can often be managed by utilizing extended-release products, taking with food and managing patient expectations (symptoms typically resolve after 2 weeks)
   - Recommend 50% dose reduction if eGFR <45 mL/min, discontinue use if eGFR <30 mL/min
   - Monitor B12 levels in patients on chronic therapy, especially if positive for neuropathy

   → ***Reminder***
   Least expensive formulation of extended release metformin = **generic Glucophage® XR**

   Avoid generic Glumetza® (modified release) and generic Fortamet® (osmotic release)

2. **Selection of subsequent agents should be patient-centered:** *See page 2 for details*
   - Consider efficacy, comorbidities (ASCVD, CHF or CKD), hypoglycemic risk, impact on weight, side effects, cost and patient preferences
   - **See page 2** for a detailed treatment algorithm

3. **Avoid the use of GLP-1 agonists and DPP-4 inhibitors in combination:** *Click here for details*
   - Use in combination is associated with minimal additive therapeutic benefit (A1C reduction ~0.3%), may be associated with enhanced risk of serious side effects (e.g., pancreatitis), increases patient and health system costs and is not a recommended combination by the ADA

4. **High baseline A1C may require early intensification of therapy:**
   - Consider insulin therapy ± other agents if newly diagnosed, markedly symptomatic and/or A1C is ≥10%
   - Once glucose toxicity is resolved consider therapy de-escalation and use of non-insulin agents especially in ASCVD

5. **If A1C remains above target on dual/triple therapy consider GLP-1 before insulin:** *Click here for details*
   - If A1C retains above target after addition of GLP-1, add basal insulin, and later prandial insulin in a stepwise fashion
   - If A1C is >11% or patient is symptomatic, insulin is the preferred injectable

6. **When insulin is indicated, consider costs:** *Click here for details*
   - Basal insulin analogs do not differ substantially in their glucose-lowering ability
   - Patients often struggle to afford insulin; consider cost-effective agents (Basaglar®, ReliOn® NPH, or insulin lispro)

7. **Limit BG testing to certain patients:** *Click here for details*
   - Avoid ordering daily BG testing in T2DM patients who are not on insulin or sulfonylureas due to limited clinical benefit, increased patient burden, added cost and potential for waste & fraud
   - May be useful to occasionally check fasting and 2h postprandial glucose levels to guide future therapeutic decisions

T2DM Treatment Algorithm

Adapted from 2019 ADA Standards of Care in Diabetes

To avoid clinical inertia, reassess and modify treatment regularly (every 3-6 months)

First-line treatment = metformin and comprehensive lifestyle modifications

OR

Established ASCVD or CKD

ASCVD Predominates

GLP-1[a] with proven CVD benefit
OR
SGLT-2i[b] with proven CVD benefit (if eGFR adequate)

⇩

HbA1c > goal after adequate trial or unable to tolerate

⇩

Choose agent demonstrating CV safety:

- Other class with CV benefit (GLP-1 or SGLT-2i)
- DPP-4i (if NOT on GLP-1)
- Basal insulin (U100 glargine or degludec)
- TZD
- SFU (later generation)

CHF or CKD Predominates

Preferably SGLT-2i[c] with proven reduction in HF or CKD progression (if eGFR adequate)
OR
GLP-1 with proven CVD benefit if SGLT-2i not tolerated or eGFR inadequate

** Avoid TZD in setting of HF **

⇩

HbA1c > goal after adequate trial

⇩

Choose agent demonstrating CV safety:

- Other class with CV benefit (GLP-1 or SGLT-2i)
- DPP-4i other than saxagliptin (if NOT on GLP-1)
- Basal insulin (U100 glargine or degludec)
- SFU (later generation)

Without established ASCVD or CKD

Compelling Need: Minimize Hypoglycemia

GLP-1 | SGLT-2i | DPP-4i | TZD

⇩

HbA1c > goal after adequate trial

⇩

SGLT-2i	GLP-1	SGLT-2i	SGLT-2i
OR TZD	**OR** DPP-4i **OR** TZD	**OR** TZD	**OR** GLP-1 **OR** DPP-4i

⇩

HbA1c > goal after adequate trial

⇩

Continue with addition of agents as outlined above

⇩

HbA1c > goal after adequate trial

⇩

Consider addition of later-generation SFU **OR** basal insulin (degludec/glargine)

Compelling Need: Minimize Weight Gain/Promote Weight Loss

GLP-1[d] with good efficacy for weight loss[+]
OR
SGLT-2i

⇩

HbA1c > goal after adequate trial

⇩

SGLT-2i or GLP-1 (whichever has not been tried)

⇩

HbA1c > goal after adequate trial

⇩

If additional therapy is required, consider DPP-4i (***if NOT on GLP-1***)

If DPP-4i is contraindicated/not tolerated, consider cautious addition of SFU, TZD **OR** basal insulin

Compelling Need: Minimize Cost

SFU **OR** TZD

⇩

HbA1c > goal after adequate trial

⇩

TZD **OR** SFU

⇩

HbA1c > goal after adequate trial

⇩

Basal insulin therapy with lowest acquisition cost
OR
Consider DPP-4i or SGLT-2i with lowest acquisition cost

Note: other low cost meds include acarbose, repaglinide or nateglinide

[a]Strongest evidence: liraglutide (Victoza®), dulaglutide (Trulicity®)> semaglutide (Ozempic®) > exenatide ER (Bydureon®); [b]empagliflozin (Jardiance®, dapagliflozin (Farziga®), canagliflozin (Invokana®); [c]Empagliflozin (Jardiance®) and canagliflozin (Invokana®); [d]semaglutide (Ozempic®) > liraglutide (Victoza®) > dulaglutide (Trulicity®) > exenatide (Byetta®) > lixisenatide (Adlyxin®)