AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGY

AACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

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AACE

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COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

PRINCIPLES OF THE AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

1.	Lifestyle modification underlies all therapy (e.g., weight control, physical activity, sleep, etc.)
2.	Avoid hypoglycemia
3.	Avoid weight gain
4.	Individualize all glycemic targets (A1C, FPG, PPG)
5.	Optimal A1C is ≤6.5%, or as close to normal as is safe and achievable
6.	Therapy choices are patient centric based on A1C at presentation and shared decision-making
7.	Choice of therapy reflects ASCVD, CHF, and renal status
8.	Comorbidities must be managed for comprehensive care
9.	Get to goal as soon as possible—adjust at ≤3 months until at goal
10.	Choice of therapy includes ease of use and affordability
11.	CGM is highly recommended, as available, to assist patients in reaching goals safely

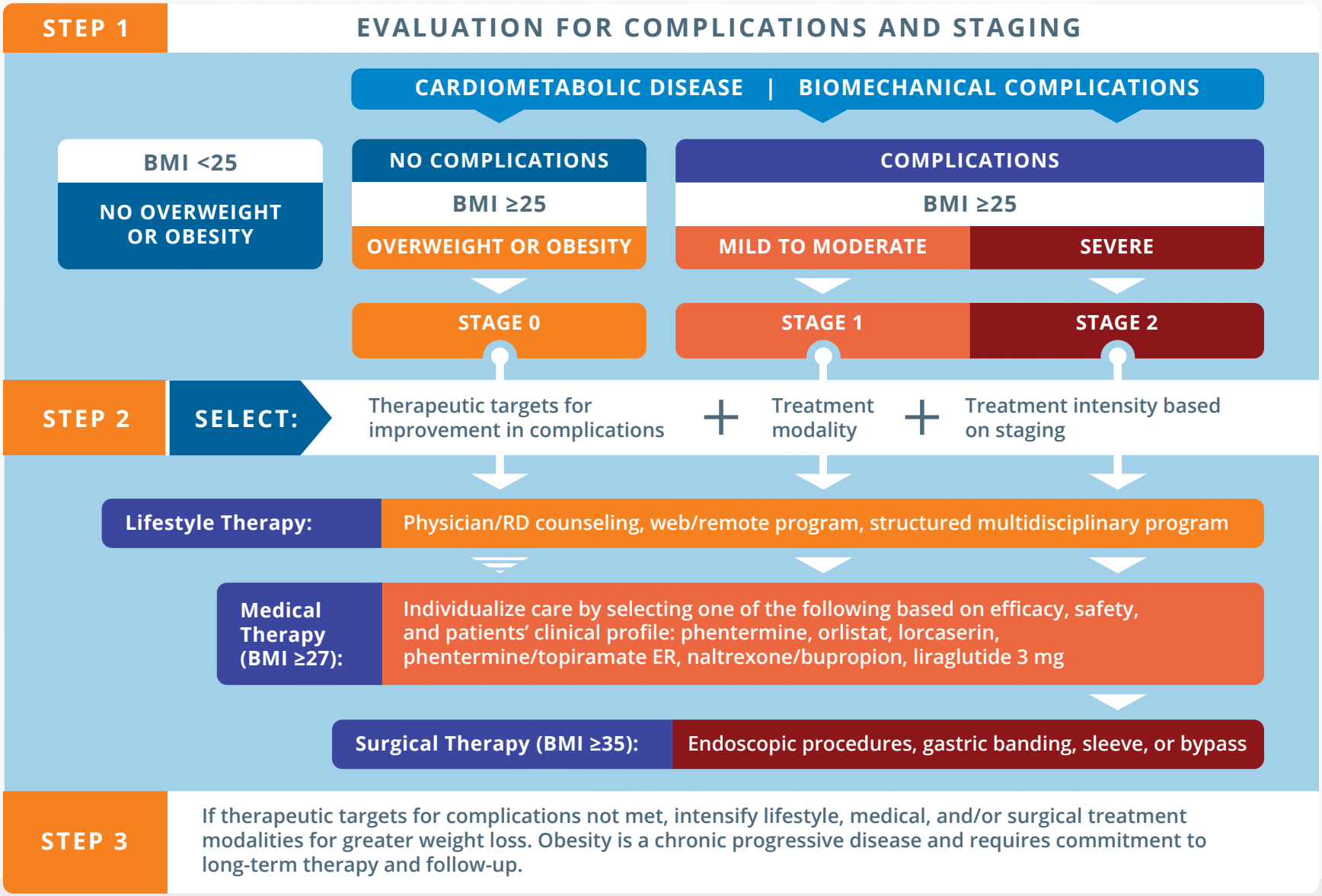
LIFESTYLE THERAPY

RISK STRATIFICATION FOR DIABETES COMPLICATIONS

INTENSITY STRATIFIED BY BURDEN OF OBESITY AND RELATED COMPLICATIONS

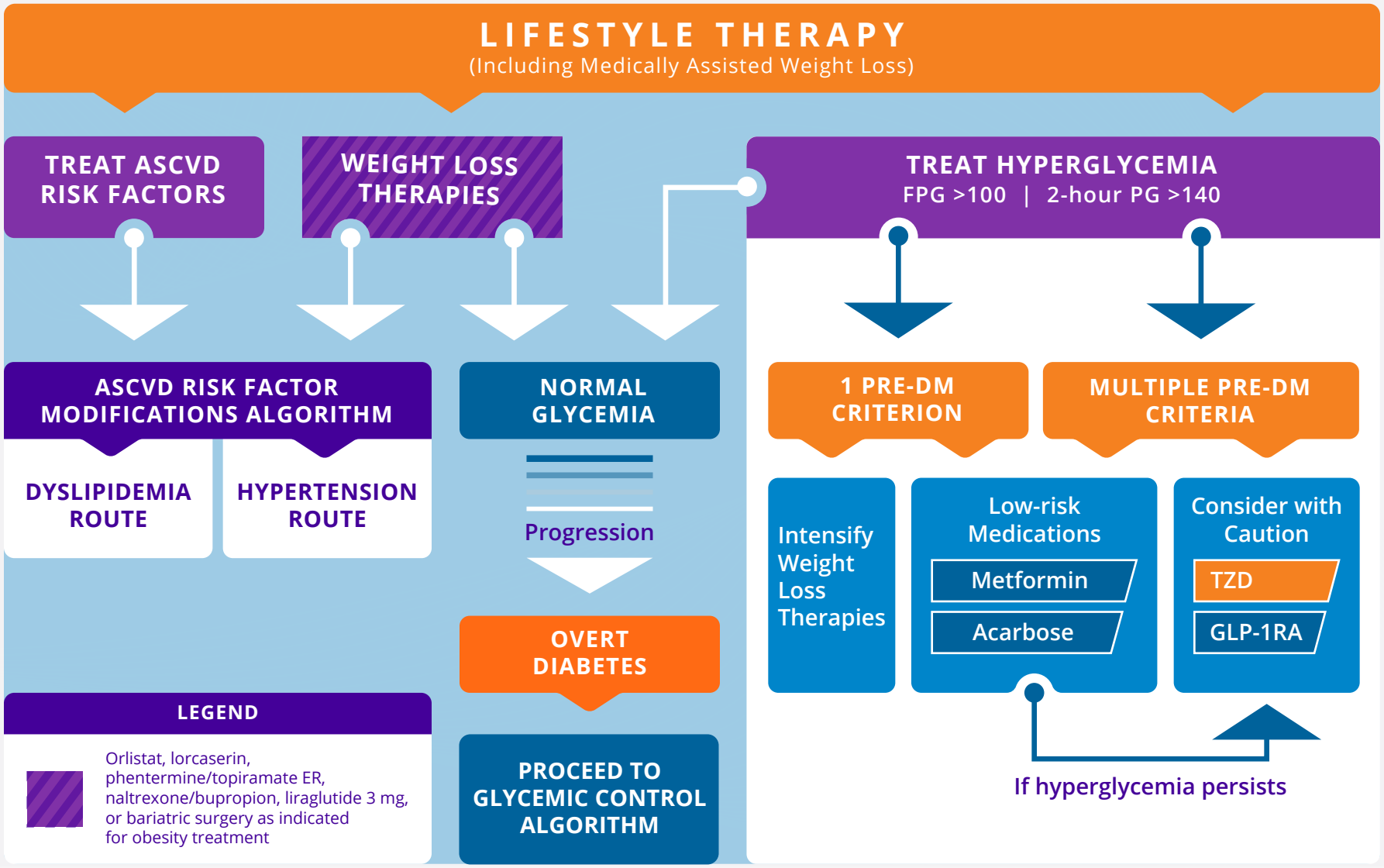
Nutrition	• Maintain optimal weight • Calorie restriction (manage increased weight) • Plant-based diet; high polyunsaturated and monounsaturated fatty acids	• Avoid *trans* fatty acids; limit saturated fatty acids • Technological aids	• Structured counseling • Meal replacement
Physical Activity	• 150 min/week moderate exertion (e.g., walking, stair climbing) • Strength training • Increase as tolerated	• Structured program • Wearable technologies	• Medical evaluation/ clearance • Medical supervision
Sleep	• About 6-8 hours per night • Basic sleep hygiene	• Screen sleep disturbances • Home sleep study	• Referral to sleep study
Behavioral Support	• Community engagement • Alcohol moderation	• Discuss mood with HCP	• Formal behavioral therapy
Smoking Cessation	• No tobacco products	• Nicotine replacement therapy and medications as tolerated	• Referral to structured program

COMPLICATIONS-CENTRIC MODEL FOR CARE OF THE PATIENT WITH OVERWEIGHT/OBESITY (ADIPOSITY-BASED CHRONIC DISEASE)



PREDIABETES ALGORITHM

IFG (100–125) | IGT (140–199) | METABOLIC SYNDROME (NCEP 2001)



ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

DYSLIPIDEMIA

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

LIPID PANEL: Assess ASCVD Risk

STATIN THERAPY
If TG >500 mg/dL, fibrates, Rx-grade OM-3 fatty acids, niacin

If statin-intolerant

Try alternate statin, lower statin dose or frequency, or add nonstatin LDL-C- lowering therapies

Repeat lipid panel; assess adequacy, tolerance of therapy

Intensify therapies to attain goals according to risk levels

RISK LEVELS	HIGH	VERY HIGH	EXTREME
	DESIRABLE LEVELS	DESIRABLE LEVELS	DESIRABLE LEVELS
LDL-C (mg/dL)	<100	<70	<55
Non-HDL-C (mg/dL)	<130	<100	<80
TG (mg/dL)	<150	<150	<150
Apo B (mg/dL)	<90	<80	<70

RISK LEVELS:
- **HIGH*:** DM but no other major risk and/or age <40
- **VERY HIGH*:** DM + major ASCVD risk(s) (HTN, Fam Hx, low HDL-C, smoking, CKD3,4)
- **EXTREME*:** DM plus established clinical CVD

If not at desirable levels: Intensify lifestyle therapy (weight loss, physical activity, dietary changes) and glycemic control; consider additional therapy

To lower LDL-C: Intensify statin, add ezetimibe, PCSK9i, colesevelam, or niacin
To lower Non-HDL-C, TG: Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin
To lower Apo B, LDL-P: Intensify statin and/or add ezetimibe, PCSK9i, colesevelam, and/or niacin
To lower LDL-C in FH:** Statin + PCSK9i

If TG 135-499: Add icosapent ethyl 4 g/day if high ASCVD risk on maximally tolerated statins

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

* EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED ** FAMILIAL HYPERCHOLESTEROLEMIA

HYPERTENSION

GOAL: SYSTOLIC <130, DIASTOLIC <80 mm Hg

ACEi or ARB

For initial blood pressure >150/100 mm Hg:
DUAL THERAPY

ACEi or ARB + Calcium Channel Blocker ✓ / ß-blocker ✓ / Thiazide ✓

If not at goal (2–3 months)

Add calcium channel blocker, ß-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, aldosterone antagonist)

Achievement of target blood pressure is critical

GLYCEMIC CONTROL ALGORITHM

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

LIFESTYLE THERAPY AND ONGOING GLUCOSE MONITORING (CGM preferred)

INDEPENDENT OF GLYCEMIC CONTROL, IF ESTABLISHED OR HIGH ASCVD RISK AND/OR CKD, RECOMMEND SGLT2i AND/OR LA GLP1-RA

Entry A1C <7.5%

MONOTHERAPY[1,2]

- ✓ Metformin
- ✓ GLP1-RA
- ✓ SGLT2i
- ✓ DPP4i
- ⚠ TZD
- ✓ AGi
- ⚠ SU/GLN

Independent of glycemic control, if established ASCVD or high risk, CKD 3, or HFrEF, start LA GLP1-RA or SGLT2i with proven efficacy*

Entry A1C ≥7.5% - 9.0%

DUAL THERAPY[1]

- ✓ GLP1-RA
- ✓ SGLT2i
- ✓ DPP4i
- ⚠ TZD
- ⚠ SU/GLN
- ⚠ Basal Insulin
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi

3 MONTHS[2]

TRIPLE THERAPY[1]

- ✓ GLP1-RA
- ✓ SGLT2i
- ⚠ TZD
- ⚠ SU/GLN
- ⚠ Basal Insulin
- ✓ DPP4i
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi

3 MONTHS[2]

MET + or other agent

Entry A1C >9.0%

SYMPTOMS

NO **YES**

DUAL Therapy OR **TRIPLE Therapy**

INSULIN ± Other Agents

ADD OR INTENSIFY INSULIN

Refer to Insulin Algorithm

LEGEND

- ✓ Few adverse events and/or possible benefits
- ⚠ Use with caution

1 Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation

2 If not at goal in 3 months, proceed to next level therapy

*CKD 3: canagliflozin; HFrEF: dapagliflozin

CKD 3 = stage 3 chronic kidney disease; HFrEF = heart failure with reduced ejection fraction; LA = long-acting (≥24 hour duration)

PROGRESSION OF DISEASE

ALGORITHM FOR ADDING/INTENSIFYING INSULIN

START BASAL (Long-Acting Insulin)

A1C <8%

TDD 0.1–0.2 U/kg

A1C >8%

TDD 0.2–0.3 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%

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

***Glycemic Goal:**

- <7% for most patients with T2D; 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

Glycemic Control Not at Goal*

INTENSIFY (Prandial Control)

Add GLP1-RA

Or SGLT2i
Or DPP4i

Add Prandial Insulin

Basal Plus 1, Plus 2, Plus 3

- Begin prandial insulin before largest meal
- If not at goal, progress to injections before 2 or 3 meals

Start: 10% of basal dose or 5 units

Basal Bolus

- Begin prandial insulin before each meal
- 50% Basal / 50% Prandial TDD 0.3–0.5 U/kg

Start: 50% of TDD in three doses before meals

Insulin titration every 2–3 days to reach glycemic goal:

- Increase prandial dose by 10% or 1-2 units if 2-h postprandial or next premeal glucose consistently >140 mg/dL
- If hypoglycemia, reduce TDD basal and/or prandial insulin by:
  - BG consistently <70 mg/dL: 10% - 20%
  - Severe hypoglycemia (requiring assistance from another person) or BG <40 mg/dL: 20% - 40%

PROFILES OF ANTIHYPERGLYCEMIC MEDICATIONS

	MET	GLP1-RA	SGLT2i	DPP4i	AGi	TZD (moderate dose)	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/Severe / Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL / GU	Contra-indicated if eGFR <30 mL/min/1.73 m^2	Exenatide Not Indicated CrCl <30 Potential Benefit of LA GLP1-RA	Not Indicated for eGFR <45 mL/min/1.73 m^2 See #1 Genital Mycotic Infections Potential CKD Benefit; See #1	Dose Adjustment Necessary (Except Linagliptin) Effective in Reducing Albuminuria	Neutral	Neutral	More Hypo Risk	Neutral	Neutral	More Hypo Risk	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF	Neutral	Neutral	Prevent HF Hospitalization Manage HFrEF; See #2	See #4	Neutral	Moderate	Neutral	Neutral	Neutral	CHF Risk	Neutral
CARDIAC ASCVD		Potential Benefit of LA GLP1-RA	See #3			May Reduce Stroke Risk	Possible ASCVD Risk	Lowers LDL-C	Safe	Neutral	
BONE	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate Fracture Risk	Neutral	Neutral	Neutral	Neutral	Neutral
KETOACIDOSIS	Neutral	Neutral	DKA Can Occur in Various Stress Settings	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

- Few adverse events or possible benefits
- Use with caution
- Likelihood of adverse effects

1. Canagliflozin indicated for eGFR ≥30 mL/min/1.73 m^2 in patients with CKD 3 + albuminuria.
2. Dapagliflozin—potential primary prevention of HF hospitalization & demonstrated efficacy in HFrEF.
3. Empagliflozin—FDA approved to reduce CV mortality. Canagliflozin—FDA approved to reduce MACE events.
4. Possible increased hospitalizations for heart failure with alogliptin and saxagliptin.

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