What You As a Cardiologist Need to Know to Use These Drugs Safely and Effectively in Your Practice

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Outline

- Key principles if adding a GLP-1RA
- Key principles if adding an SGLT-2i
- Engagement of other key personnel
  - pharmacy, nursing, CDE, diabetologist

Adding a GLP-1RA

Generic	Trade Name	CV Outcomes Trial	Results Available
lixisenatide	Adlyxin	ELIXA	2015
liraglutide	**Victoza**	**LEADER**	**2016**
semaglutide	**Ozempic**	**SUSTAIN-6**	**2016**
exenatide	Bydureon	EXSCEL	2017
dulaglutide	**Trulicity**	**REWIND**	**2019**

Adding a GLP-1RA

- Adjustments to other medications:
  - Cease DPP4 inhibitor: no synergistic benefit, expensive.
  - If HbA1c is:
    - ‘controlled’ (i.e. <7%), consider:
      - Decrease SU by 50%
      - Reduce basal insulin by 20%
    - not ‘controlled (i.e. >7%), no need to adjust SU/insulin

Start GLP-1 RA and engage diabetes care provider to assess glycemic response, make additional medication adjustments.

GLP-1 RA doses generally require up-titration for effectiveness

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Adding a GLP-1RA (2)

- Anticipate nausea and vomiting:
  - Related to GLP-1 activity → slow gastric motility → satiety
  - Eat slowly, avoid large meals
  - Start at lowest dose
    - Up-titrate if needed for additional glycemic control
    - Start low, go slow! Most settle on a stable dose at 2 weeks.
- Administration education
  - Consider:
    - training up practice nursing staff to assist
    - Referral to local pharmacist for education
    - Referral back to diabetes care provider if not feasible

Adding an SGLT-2i

Generic	Trade Name	CV Outcomes Trial	Results Available
empagliflozin	Jardiance	EMPA-REG	2015
canagliflozin	Invokana	CANVAS	2017
dapagliflozin	Farxiga	DECLARE	2018
ertugliflozin	*Steglatro*	*VERTIS*	*Q2 2020*

Adding an SGLT-2i

- Adjustments to other medications:
  - Volume status and blood pressure?
    - Dry or borderline hypotensive: halve diuretic, reduce anti-HTN
    - Euvolemic and/or normotensive: anticipatory guidance
  - If HbA1c is:
    - ‘controlled’ (i.e. <7%), consider:
      - Decrease SU by 50%
      - Reduce basal insulin by 20%
    - not ‘controlled (i.e. >7%), no need to adjust SU/insulin

Safety considerations

- Key safety considerations:
  - Amputation:
    - Observed in CANVAS, not in CREDENCE or other CVOTs
    - Avoid commencement in ‘active’ foot infection
  - Fournier’s gangrene
    - Rare, but FDA label.
    - Avoid in high risk severe GU infection (chronic incontinence, unable to perform perineal hygiene)
  - eGFR:
    - Not a safety issue, but one of efficacy…

Dosing with kidney dysfunction

Generic	Trade Name
empagliflozin	Contraindicated eGFR <**45** ml/min/1.73m^2
canagliflozin	*Expanded indication – see next slide*
dapagliflozin	Not recommended for eGFR <**45** ml/min/1.73m^2; contraindicated if eGFR<30 ml/min/1.73m^2
ertugliflozin	Initiation not recommended for eGFR <**60**ml/min/1.73m^2

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Dosing with kidney dysfunction

Table 1: Recommended Dosage

estimated glomerular filtration rate eGFR (mL/min/1.73 m^2)	Recommended Dosage
eGFR ≥ 60	100 mg orally once daily, taken before the first meal of the day. Dose can be increased to 300 mg once daily for additional glycemic control.
eGFR 45 to < 60	100 mg once daily.
eGFR 30 to < 45*	
On dialysis	Contraindicated *[see Contraindications]*.

* with albuminuria >300 mg/day.

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Safety considerations

Euglycemic DKA…

- Uncommon
- Atypical presentation
  - "euglycemic DKA" – less than expected hyperglycemia
  - Reduced/absent ketonuria
  - May delay diagnosis
- If clinical suspicion for DKA
  - i.e. N/V, malaise, abdominal pain, confusion, etc.
  - Check anion gap, serum ketones (βOHB), arterial pH
  - Stop the SGLT2-i

Tips to avoid DKA

Predisposing factor	Management
Acute illness, diarrhea, MI	Withhold at onset, restart when well and tolerating PO
Major surgery	Withhold at least 3 days prior Restart when euvolemic and tolerating PO.
Volume depleted states (i.e. colonoscopy preparation)	Withhold
Excessive alcohol intake	Stop immediately, restart when tolerating PO intake

Know your limits

When to engage a diabetologist?

- Very complex existing regimen:
  - Combination insulin regimen (basal-bolus, mixed preparations)
  - ≥ 3 oral anti-hyperglycemic medications
- History of severe or recurrent hypoglycemia
- Prior DKA
- Active diabetic foot wound
- To follow up glycemic response, drug tolerability and further adjust regimen

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