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PREAMBLE

Calgary Zone LTC P&T Committee decided to list empagliflozin, dapagliflozin, sitagliptin, and linagliptin with restrictions under Special Authorization for the following reasons:

- For many LTC residents living with diabetes, glycemic goals may not be achievable on monotherapy with metformin.
- Individualized glycemic targets should be **frequently** reassessed due to advancing frailty with a thoughtful consideration of the balance of harm vs. benefits of tighter glycemic control.
- The committee has been monitoring utilization and evidence over the last several years. We are seeing broader and increased use of these agents in the community and LTC.
- There is utility in using these agents to simplify complex insulin regimens and to reduce frequent blood glucose monitoring when using prandial insulin, and repaglinide.
- Long-term sustainability of drug funding and budget constraints were considered.
- The Canadian Agency for Drugs and Technologies in Health (CADTH) and Canadian Drug Expert Committee (CDEC) systematically reviewed the options available as second-line/add-on when metformin is no longer sufficient to manage type 2 diabetes. In assessing for clinical effectiveness and cost-effectiveness, they recommend that for patients *with* established cardiovascular (CV) disease, empagliflozin can be added to metformin, however for patients *without* CV disease, a sulfonylurea still provides the best value for payers in terms of quality-of-life years (QALY) gained, particularly for patients with lower risk of hypoglycemia. For patients with a high risk of hypoglycemia, empagliflozin follows in terms of QALY gained. For additional CADTH CDEC recommendations for empagliflozin and dapagliflozin, see their Common Drug Review Reports.

ASSESSMENT

Appropriateness is assessed on a case-by-case basis and shall include a thoughtful review of the resident's current health status and Goals of Care Designation. Other factors for consideration are:

- Resident's goals for drug therapy
- Assessment of frailty and medication burden
- RAI-MDS (Resident Assessment Instrument – Minimum Data Set) 2.0 outcome scales (e.g. Changes in Health, End-Stage Disease and Signs and Symptoms [CHESS] and Personal Severity Index [PSI], etc.)
- Recent Blood Glucose (BG) readings

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- Hypoglycemia risk
- Consultations with specialists (e.g. endocrinology, cardiology, internal medicine, etc.)
- Duration of illness and comorbid conditions, time-to-benefit
- Volume status and renal function, risk of erratic or inadequate fluids consumption (e.g. dementia, fluid restricted diet, etc.)
- Risk of genital and UTI infection
- **Strong consideration for deprescribing, regimen simplification and de-escalation with advancing frailty**
    - An example of an insulin regimen simplification can be found in the American Diabetes Association's *Older Adults: Standards of Medical Care in Diabetes – 2023*, -Figure 13.1. Simplification of Complex Insulin Therapy.

PROTOCOLS

Protocol 1 – Empagliflozin, dapagliflozin, sitagliptin, or linagliptin for Type 2 Diabetes (with no established CV disease)

As add-on therapy for residents with Type 2 diabetes who meet the following criteria:

1. On maximally tolerated dose of metformin (formulary first-line agent), AND
2. On maximally tolerated dose of sulfonylurea or repaglinide (formulary second-line agents), unless contraindicated or resident is at risk for severe hypoglycemia[1], AND
3. Formulary first and second-line agents are insufficient to meet personalized glycemic targets.
4. Insulin Consideration:
    - In adults with Type 2 Diabetes, when glycemic targets are not met with formulary first- and second-line oral agents +/- basal insulin, adding or continuing a DPP-4 inhibitor can reduce the need to increase basal insulin or add bolus insulin.

[1] Risk factors for severe hypoglycemia: prior episode of severe hypoglycemia, current low A1C (<6%), hypoglycemia unawareness, long duration of insulin use, autonomic dysfunction, CKD, cognitive impairment, unable to respond to mild hypoglycemia on their own, low health literacy, low economic status, food insecurity. Lipsombe L, Booth G, Butalia S, Dasgupta K, et al. *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*: Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Can J Diabetes 2018;42(Suppl 1):S88-S103.

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- Hospital transfers: Acute care often uses insulin for timely glycemic management in hospital. Often, oral medications are held or stopped while receiving in-patient care. On admission/transfer to LTC, insulin regimens should be reassessed.

Exclusions:

1. DPP-4s are excluded when resident is taking prandial insulin.
2. DPP-4s are excluded when resident is using a GLP-1 analog. GLP-1 analogs are non-formulary.

Protocol 2 – empagliflozin or dapagliflozin for Type 2 Diabetes with Cardiovascular Disease (including heart failure) or chronic kidney disease.

As add-on therapy for residents with Type 2 diabetes who meet the following criteria:

1. On a maximally tolerated dose of metformin (or those unable to take metformin), **AND**
2. Have inadequate glycemic control according to resident's individualized glycemic targets*, **AND**
3. Have a qualifying cardiovascular condition** or albuminuric chronic kidney disease.

Protocol 3-dapagliflozin for heart failure

As add-on therapy for residents with heart failure with reduced ejection fraction (HFrEF) who meet the following criteria:

1. Reduced left ventricular ejection fraction (LVEF) (less than or equal to 40%), AND
2. New York Heart Association (NYHA) class II or III HF symptoms, AND
3. When used as adjunctive therapy to standard therapy including:
   - a stable dose of an angiotensin converting enzyme inhibitor (ACEI) OR angiotensin II receptor antagonist (ARB), AND a beta-blocker, AND, if tolerated, a mineralocorticoid receptor antagonist (MRA)

Clinicians are referred to the Health Canada product monograph(s) for approved indications and limitations to use, prescribing and monitoring information.

Submission Process

Requests for coverage will be submitted using Special Authorization Form (SA-30). For residents newly admitted or readmitted from hospital, form submission is required withing 3 weeks (grace period). For new starts, form submission is required prior to initial drug provision. The distribution of the form to pharmacy providers will be via email.

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Monitoring and Duration of Coverage

The risk/benefit assessment, including review of resident's goals, shall occur initially and annually, or more often as necessary. Appropriate laboratory indices shall be monitored to assess disease status and renal function. If there is a significant decline in health status, the benefit and ongoing use of the medication should be reassessed. The clinical pharmacist shall document their assessment and any resulting recommendations in the resident's chart.

Coverage Duration: One year. Annual form submission is required for renewal.

Qualifying cardiovascular conditions

Presence of one or more of the following (plus type 2 diabetes):

- History of MI
- Multi-vessel coronary artery disease in two or more major coronary arteries (irrespective of revascularization status)
- Single-vessel coronary artery disease with significant stenosis and either a positive non-invasive stress test or discharged from hospital with a documented diagnosis of unstable angina within 12 months prior to selection
- Last episode of unstable angina > 2 months prior with confirmed evidence of coronary multi-vessel or single-vessel disease
- History of ischemic or hemorrhagic stroke
- Occlusive peripheral artery disease
- Heart Failure

Glycemic Targets

Clinicians are referred to current clinical practice guidelines to guide the selection of individualized glycemic targets. Of particular interest to the population in LTC is a set of guidelines developed by PATH (Palliative and Therapeutic Harmonization) that take into account frailty-specific recommendations for Type 2 Diabetes. For residents living with severe, very severe, or terminally ill frailty (scores of 7-9 on the Clinical Frailty Scale), the guidelines recommend to "maintain HbA1c at or above 8% rather than below a specific level, in keeping with the conclusion that lower HbA1c levels are associated with increased hypoglycemic events without accruing meaningful benefit for frail older adults with type 2 diabetes." See link for complete recommendations.

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Guideline Links

Diabetes Canada Clinical Practice Guidelines

References

CADTH. *New Drugs for Type 2 Diabetes: Second-Line Therapy – Recommendations Report.* Ottawa: 2017 May. (CADTH therapeutic review; vol.4, no 1c).

CADTH. *CADTH CDEC Final Recommendation: Empagliflozin (Jardiance – Boehringer Ingelheim (Canada) Ltd.) Indication: Type 2 Diabetes Mellitus*. Ottawa: 2015.

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