Clinical Endpoints Review:

Devices for Self-management of Type 1 and Insulin-Dependent Type 2 Diabetes

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Agenda

10:00 – 10:10	**Welcome and Introduction**
10:10 – 10:30	**MEDCAC Administrative Issues** • Purpose of the Subcommittee/Roles and Expectations • Structure and conduct of the MEDCAC • Review of FACA requirements
10:30 – 10:50	**Summary of the Clinical Endpoints Review**
10:50 – 11:00	**BREAK**
11:00 –12:00	**Discussion Questions** • Did the CER capture the appropriate literature? • Are outcome domains appropriate? • Are the surrogate/clinical and non-clinical endpoints appropriate? • Are the quality-of-life instruments appropriate? • What are minimal clinically important differences (MCID) for the identified endpoints?
12:00 – 12:30	**LUNCH**
12:30 – 2:00	**Discussion/Refinement of Draft Voting Questions**

CER Overview: Glycemic Control

- Two key measures
  - (Hb)A1c: % red blood cells with sugar-coated hemoglobin. Usually averaged over the past 3 months
  - Glycemic variation, i.e., incidence of hyper-/hypoglycemia
- Optimal blood glucose range: 70-180 mg[of sugar]/dL[of blood]
- Hypoglycemia: key issue for older adults
  - Hospital admission rates for hypoglycemia > those for hyperglycemia
  - Dizziness, weakness, trouble speaking, confusion
- Hyperglycemia: can cause ketoacidosis

CER Overview: Devices for Management of Diabetes

- Appropriate for patients with Type 1 or insulin-dependent Type 2 diabetes
- Devices included in the CER
  - Continuous glucose monitors (CGMs)
  - Insulin pumps
  - Closed loop systems (CLS),
    - Also called ‘hybrid closed-loop systems’, ‘automated insulin delivery systems’, ‘bionic pancreas’, ‘artificial pancreas’
    - CLS devices incorporate a CGM

CER Methods

- Searched published literature (Embase and PubMed databases), 2018-2023
- Collected research reports on the 3 device types
- Included
  - Systematic reviews of clinical studies
  - Formal consensus statements
  - Prospective clinical studies (RCTs, nonrandomized, single-arm)
- Excluded
  - Case report/case series, cross-sectional, case-control
  - Retrospective
  - Prospective observational studies
- Selection criteria matter if important endpoints/outcomes were missed – Subcommittee may add omissions to the voting questions

Summary of CER Findings

Tables A1, A2 and B in Review Packet

Discussion Questions and Response from Endocrinologist Review

1. Did the CER capture the **appropriate literature?**

Hwang: Yes

2. Are the endpoint **domains** appropriate?

Hwang: Yes. Another useful outcome/domain would be device accuracy. MARDs (mean absolute relative differences from a reference standard) of CGMs are high in the hypoglycemic range.

3. Are the **surrogate/clinical** endpoints (A1c, hypoglycemia, etc. in Table A1 of the review packet) appropriate?

Hwang: a) Agree on A1C; level 1, 2 and 3 hypoglycemia; and level 2 hyperglycemia as key endpoints for older adults.
b) Agree with emphasis on hypoglycemia, as opposed to A1c and time in range, in older adults.
c) 70 mg/dL is a pragmatic definition of hypoglycemia.

4. Are the **other endpoints** listed in Table A1 appropriate (**QOL, healthcare resource use, serious adverse events, adverse events**)?

Hwang: Yes. Suggest adding sleep disturbance. Safety/adverse events should always be key endpoints.

5. Are the QOL instruments identified in the CER appropriate?

Hwang: Add measures of hypoglycemia awareness (Gold Score, Hypo-A-Q)

6. Can you offer definitions of a **MCID for the surrogate/clinical endpoints** that you designated to be key endpoints in response to question #3?

Hwang: a) Reduction in level 2 hyperglycemia by 10% [hypothetical example in the review packet] would be clinically important.
b) 0.5% change in A1C has been defined previously as being an MCID [Lenters-Westra 2014??].

Mock Voting Questions

Separate document