Oral Semaglutide for Type 2 Diabetes: Final Policy Recommendations

December 9, 2019

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the November 14, 2019 New England CEPAC public meeting on the use of oral semaglutide for the treatment of Type 2 diabetes. At the meeting, ICER presented the findings of its revised report on these treatments and the New England CEPAC voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations, and long-term value for money at current prices. Following the votes, ICER convened a Policy Roundtable of one patient advocate, two clinical experts, two payers, and three representatives from pharmaceutical manufacturers to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed here, https://www.youtube.com/watch?v=BBswZtaiRt0&feature=youtu.be, immediately followed the New England CEPAC voting portion of the meeting. More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the appendix of this document. ICER's report on these treatments, which includes the same policy recommendations, can be found here https://icer-review.org/meeting/type-2-diabetes-2/.

The roundtable discussion was facilitated by Dr. Steven Pearson, MD, MSc, President of ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

Manufacturers

Manufacturers with new agents for diabetes mellitus should seize the opportunity to come to market with a lower list price to benefit patients.

We heard about how financial toxicity has led to poor patient outcomes as patients underdose certain therapies to reduce costs. Manufacturers can reduce financial toxicity for many uninsured patients with lower list prices, and employers and PBMs can benefit patients by passing along net price savings to patients.

To provide high quality head-to-head evidence on the comparative effectiveness of emerging treatment options for patients with diabetes, manufacturers should look to the example set by the PIONEER trials of oral semaglutide.

The PIONEER trials provide extensive information on the comparative effectiveness of oral semaglutide versus other relevant treatments across an appropriate spectrum of background populations and therapies. Novo Nordisk should be commended for their support of these trials.

Payers

Prior authorization criteria for antihyperglycemic products should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for submitting prior authorization material should be clear and efficient for providers. Options for specific elements of coverage criteria within insurance coverage policy are discussed below.

Patient Eligibility Criteria

a. **Diagnosis**: Inadequate control of T2DM will vary by patient age and some payers may consider looking at specific A1c criteria for control in the 2019 ADA Guidelines. This is not intended to account for any possible future indications for CV risk reduction in patients with T2DM with controlled A1c.
b. **Clinical criteria:** Given that nearly all the evidence on the effectiveness of semaglutide has come from studies of patients who have had inadequate control on metformin, payers may consider requiring attestation from clinicians that patients have had an adequate trial of metformin with A1c levels remaining above clinical targets. However, we heard from clinical experts that metformin is used nearly universally as first-line therapy and that adding a prior authorization requirement would add administrative overhead without additional benefit.
c. **Step Therapy:** We heard from payer representatives that there is very little insurer management of treatment for T2DM, but that patient resistance to injectable treatments limited the early-line use of GLP-1 therapies. This resistance will be removed with an oral GLP-1 therapy and, as a result, some payers may consider instituting step therapy. However, we heard from clinical experts that some drug classes are preferable for specific patients based on a number of interacting clinical criteria, and that a routine step through SGLT-2s or DPP-4s would be viewed as lacking clinical nuance. We heard from payer analysts that some payers have instituted a step therapy requirement for an injectable GLP-1 RA prior to receiving coverage for oral semaglutide. Clinical experts felt this was not clinically sensible. More broadly, clinical experts acknowledged that they will have some patients whom they believe would do equally well with an SGLT-2i or a GLP-1 RA, and in those cases it would be appropriate for clinicians to pick the substantially cheaper agent

(currently an SGLT-2i) given the lack of evidence demonstrating clear superiority of one therapy over the other for many patients. Payers considering step therapy with other oral agents prior to access to coverage for oral semaglutide should consult with patients and clinical experts to determine whether step therapy can be targeted to appropriate patients without undue administrative burden.

d. **Other Clinical Criteria:** We heard from clinical experts that concurrent therapy with an SGLT-2i and a GLP-1 RA is common. Some payers may wish to consider limiting an initial trial or oral therapy to one agent after metformin, but there may be considerable resistance from clinicians and patients given the lack of prior experience with active management in this disease space.
e. **Renewal Criteria:** A1c criterion for renewal would not be appropriate given benefits of oral semaglutide beyond A1c control.
f. **Prescriber Criteria**: Given the prevalence of T2DM and the safety profile for oral semaglutide, there appear to be no evidence-based reasons to consider restricting providers to specialists.

Clinicians

As the treatment options for T2DM continue to evolve, primary care providers should make themselves aware of the 2019 ADA Guidelines on treatment of T2DM to ensure that all treating clinicians know how to identify the varying risks and benefits of different agents for particular subpopulations.

Appropriate management of T2DM is changing as new medications and new evidence become available. The 2019 ADA Guidelines incorporate best evidence and provide figures that allow quick decision making when starting or adding medication therapy. It is imperative that primary care providers familiarize themselves with these guidelines. As part of this, providers should note that therapies have different benefits and harms and it is important to engage in shared decision making with patients in choosing therapies. Additionally, clinicians should remember that drug therapy is only a portion of the necessary care and education of people with diabetes.

Clinicians should not "threaten" patients with treatment with insulin if they "fail" other therapies.

Many patients with T2DM will eventually need to be treated with an insulin preparation. Many patients will have been told that if they are unable to reduce their glucose levels with lifestyle changes and oral medications, that they will be prescribed insulin, and clinicians will use the possibility of needing insulin as a motivating factor for lifestyle changes and medication adherence. This creates a fear among patients far out of proportion to the actual difficulty of insulin therapy for T2DM and causes many patients who would benefit from insulin therapy to postpone or refuse the treatment.

Researchers

Given the high rate of gastrointestinal side effects with oral semaglutide, real world evidence on adherence should be studied and reported.

An important uncertainty around oral semaglutide is whether its effectiveness in the real world will match its efficacy seen in randomized trials. Real world evidence is needed to address this issue.

It will be important to understand the relative benefits of GLP-1 RAs and SGLT-2i's on patient important outcomes such as cardiovascular events; these can likely best be assessed in head-to-head pragmatic clinical trials.

Because of the concerns around adherence, and the importance of knowing whether the "next" therapy for a patient with T2DM should be a GLP-1 RA or an SGLT-2i, head-to-head trials using pragmatic designs that can better assess effectiveness should be performed.

Trials of combination therapies, particularly of GLP-1 RAs and SGLT-2i's, should be performed.

It is currently uncertain whether combining GLP-1 RAs and SGLT-2i's achieves patient-important benefits that are additive or whether the benefits are smaller or larger than would be expected when considering these classes individually. These agents are already being used in combination, and clinical research is needed to guide appropriate practice and patient counseling.

Appendix

Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the New England CEPAC Public Meeting on November 14, 2019, in Providence, Rhode Island.

Appendix Table 1. ICER Staff and Consultants and COI Disclosures

Name	Organization	Disclosures
Pam Bradt, MD, MPH	Institute for Clinical and Economic Review	*
Eric Borrelli, PharmD, MBA	Institute for Clinical and Economic Review	*
Rick Chapman, PhD, MS	Institute for Clinical and Economic Review	*
Katherine Fazioli, BS	Institute for Clinical and Economic Review	*
Greg Guzauskas, MSPH, PhD	University of Washington	*
Ryan Hansen, PhD, PharmD	University of Washington	*
Catherine Koola, MPH	Institute for Clinical and Economic Review	*
Steve Pearson MD, MSc	Institute for Clinical and Economic Review	*
Michelle Poulin, BA	Institute for Clinical and Economic Review	*
David Rind, MD, MSc	Institute for Clinical and Economic Review	*

*No relevant conflicts of interest to disclose, defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Appendix Table 2. New England CEPAC Panel Member Participants and COI Disclosures

Name	Organization	Disclosures
Robert Aseltine Jr, PhD*	Professor and Chair, Division of Behavioral Sciences and Community Health, UCONN Health	*
Marthe Gold, MD, MPH*	Senior Scholar, New York Academy of Medicine	*
Claudio Gualtieri, JD*	Advisor, Center to Champion Nursing in America, AARP	*
Stephen Kogut, PhD, MBA, RPh*	Professor of Pharmacy Practice, University of Rhode Island College of Pharmacy	*
Greg Low, RPh, PhD*	Program Director, MGPO Pharmacy Quality and Utilization Program	*
Eleftherios Mylonakis, MD, PhD, FIDSA*	Chief of the Infectious Diseases Division and Dean's Professor of Medicine, Warren Alpert Medical School of Brown University	*
Stephanie Nichols, PharmD, BCPS, BCPP, FCCP*	Associate Professor Pharmacy Practice, University of New England College of Pharmacy	*
Leslie Ochs, PharmD, PhD, MSPH*	Associate Professor of Social and Administrative Pharmacy, University of New England College of Pharmacy	*
Brian O'Sullivan, MD*	Professor of Pediatrics, Geisel School of Medicine at Dartmouth College	*
Jason Schwartz, PhD*	Assistant Professor, Department of Health Policy and Management, Yale School of Public Health	*
Jason Wasfy, MD, MPhil*	Director, Quality and Outcomes Research, Massachusetts General Hospital Heart Center	*
Edward Westrick, MD, PhD*	Primary Care Physician, Assistant Medical Director, Comprehensive Community Action Program	*

*No relevant conflicts of interest to disclose, defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

Participant	Affiliation	Disclosures
Jeff Casberg, MS, RPh	Director of Clinical Pharmacy, IPD Analytics	Owns stock shares in Anthem, Cigna, CVS, and McKesson
Bonnie Donato, MA, PhD	Executive Director of Primary Care, Health Economics, and Outcomes Research, Boehringer Ingelheim	Full-time employee of Boehringer Ingelheim
Todd Hobbs, MD	Vice President, Chief Medical Officer of North America, Novo Nordisk	Full-time employee of Novo Nordisk
Joanna Mitri, MD, MS	Staff Endocrinologist, Joslin Diabetes Center	Received support from the National Dairy Council, National Institutes of Health, Kowa, and the Juvenile Diabetes Research Foundation. Received <$6,000 for a one-time consultation with Novo Nordisk.
Lisa Murphy, MD, DPhil	Chief, Division of Endocrinology and Metabolism, San Francisco General Hospital, University of California, San Francisco	*
David Strutton, PhD	Vice President, Global Pharmaceuticals & Policy Research, Center for Observational and Real-World Evidence, Merck	Full-time employee of Merck
Susan Weiner, MS, RDN, CDE, FAADE	Scientific Council Member, Beyond Type 2	*

*No relevant conflicts of interest to disclose, defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.