



FOCUS ON GLP-1

THE ROLE OF GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONISTS IN THE MANAGEMENT OF DIABETES

This resource provides a summary for practicing pharmacists on pharmacologic approaches to the management of both type 1 and type 2 diabetes. The focus of this resource will be on the management of type 2 diabetes, with an emphasis on the use of glucagon-like peptide-1 (GLP-1) receptor agonists.

INTRODUCTION

Diabetes impacts millions of patients, with an estimated 34.1 million adults—or 13.0% of all US adults—having diabetes, according to the Centers for Disease Control’s (CDC’s) National Diabetes Statistics Report.¹ Of these, 26.8 million have been diagnosed with the condition, with the remaining 7.3 million being undiagnosed. As patients age, the prevalence of diabetes increases, with the greatest percentage observed in patients aged 65 years or older (26.8%) followed by patients aged 45–64 years (17.5%). In addition, certain race/ethnicities such as American Indians/Alaska Natives, Hispanics, and non-Hispanic blacks have higher rates of diabetes compared with non-Hispanic whites.¹

Patients with diabetes are at an increased risk of both macrovascular and microvascular complications such as major cardiovascular (CV) events (eg, ischemic heart disease, stroke), kidney disease, retinopathy, and neuropathy.² Therefore, effective interventions aimed at maintaining individualized glycemic targets are fundamental to decreasing the risk of these complications.

The American Diabetes Association (ADA) has published glycemic targets, with A1C being the primary test to assess for glycemic control.² For the majority of nonpregnant adults, an A1C target of <7% is appropriate; however, this target may be modified based on key patient characteristics. The ADA recommends that glycemic targets be individualized in the context of shared decision-making to address the needs and preferences of each patient. Select factors that should be considered include the risks of hypoglycemia and other drug-related adverse events, disease duration, life expectancy, patient preference, and patient resources and support system.² For example, a more stringent goal (eg, <6.5%) may be considered for those who can achieve this target safely, whereas a less stringent goal (eg, <8%) may be considered for those with a high risk of severe hypoglycemia, limited life expectancy, and/or advanced complications.

GUIDANCE ON DIABETES MANAGEMENT

The 2020 ADA *Standards of Medical Care in Diabetes* provide guidance on the pharmacologic approaches to the management of both type 1 and type 2 diabetes.³ These standards are updated and published annually in the January supplement of *Diabetes Care*, and are also accessible on ADA’s website (<https://professional.diabetes.org/content-page/practice-guidelines-resources>). Sixteen sections are included which cover a broad range of topics such as the classification and diagnosis of diabetes, prevention or delay of the disease, facilitating behavior change, a newer diabetes technology section, and pharmacologic management approaches. Drug- and patient-specific factors for consideration when selecting antihyperglycemic treatments are included, along with a detailed algorithm to help guide treatment decisions. In addition, the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) have published a 2020 consensus statement on the comprehensive management of type 2 diabetes (<https://www.aace.com/pdfs/diabetes/algorithm-exec-summary.pdf>).⁴ Within this guidance, a glycemic control algorithm is also included along with profile comparisons of antihyperglycemic agents.

2020 ADA Diabetes Standards of Care: A Focus on GLP-1 receptor agonists

The focus of this resource will be on the management of type 2 diabetes, with an emphasis on the use of glucagon-like peptide-1 (GLP-1) receptor agonists. When selecting appropriate pharmacologic treatments, the ADA recommends a patient-centered approach that takes into consideration both treatment-related and patient-specific factors. Efficacy of treatments (A1C lowering), adverse events, hypoglycemia risk, effects on body weight, cost, and patient preference should all be considered.³ The presence of comorbidities such as atherosclerotic CV disease (ASCVD), indicators of high ASCVD risk, renal dysfunction (eg, chronic kidney disease [CKD], nephropathy, or both), and heart failure (HF) also play a key role in determining appropriate treatments.

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Figure 1. ADA recommendations for intensification to dual glucose-lowering therapy.³

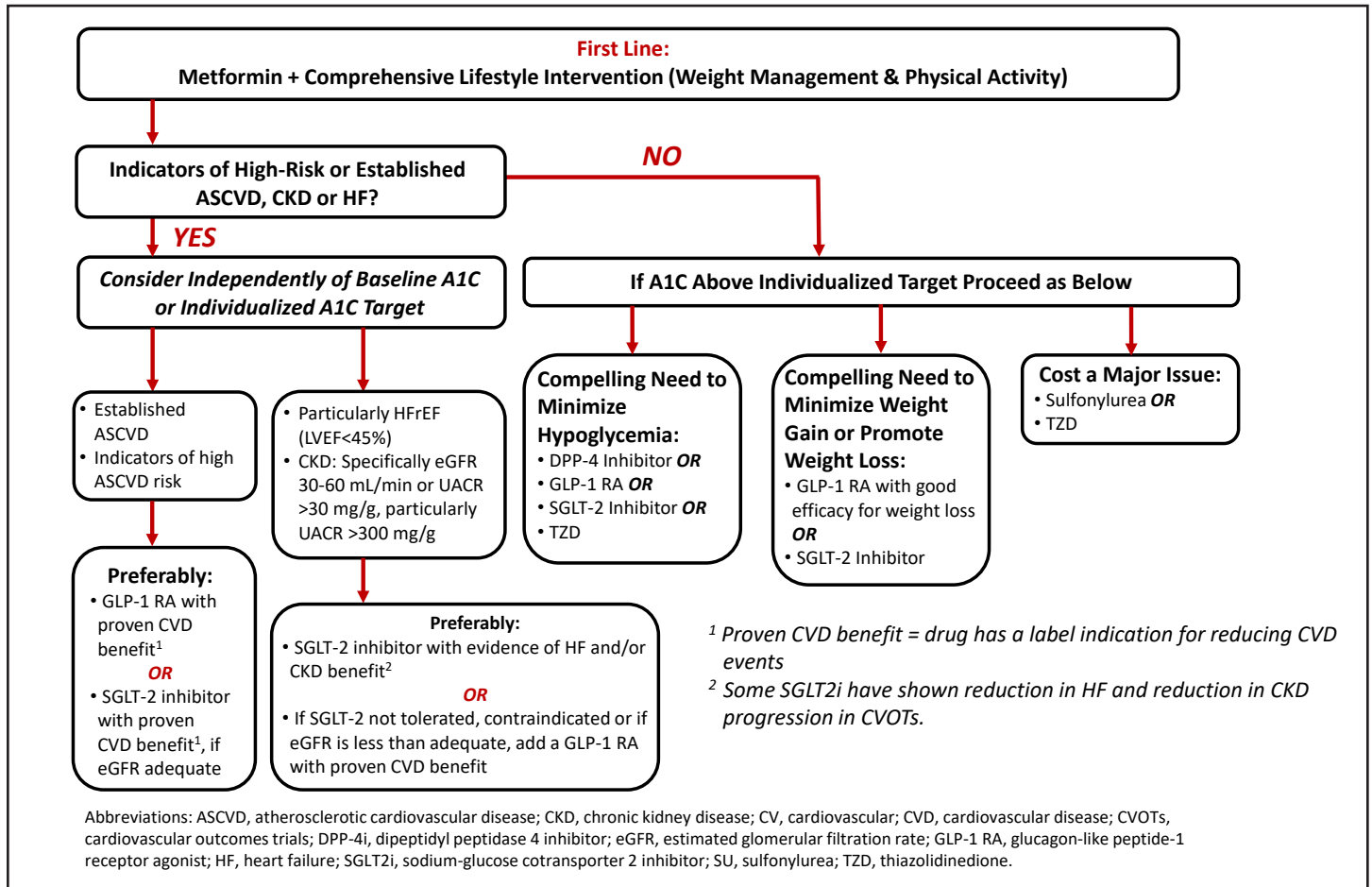


Figure 1 reflects an excerpt from American Diabetes Association. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2020. Diabetes Care. 2020;43(Suppl. 1):S98-110. Copyright and all rights reserved. Material from this publication, which can be found at https://care.diabetesjournals.org/content/43/Supplement_1/S98 has been used with the permission of American Diabetes Association.

When patients with type 2 diabetes require the use of an injectable for further glycemic control, the ADA recommends that the use of GLP-1 receptor agonists be considered when possible. “The ADA noted that this recommendation is based on GLP-1 receptor agonists having a lower risk of hypoglycemia and beneficial effects on body weight, albeit with greater gastrointestinal side effects.”³ It is important to note, however, that the ADA continues to recommend insulin as the first injectable therapy in patients where there is evidence of ongoing catabolism, symptoms of

hyperglycemia are present, when A1C levels (>10%) or blood glucose levels (≥ 300 mg/dL) are very high, or when a diagnosis of type 1 diabetes is a possibility.

Patient Communication and Counseling Pearls for Patients With Type 2 Diabetes

When starting the conversation with patients about their type 2 diabetes, the use of open-ended questions can help to assess disease control and complications, medication knowledge, medication adherence, history of adverse events (eg, hypoglycemia), patient preferences, and the patient’s lifestyle. These conversations will be beneficial in helping identify potential patients for GLP-1 receptor agonists and addressing medication- and disease-related considerations. Examples of strategies for starting the conversation with patients with type 2 diabetes are summarized in Table 2.⁵



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Table 2. Strategies for Starting the Conversation With Patients With Type 2 Diabetes

Disease control and complications	<p>How often do you check your blood sugar?</p> <p>What are your daily glucose readings?</p> <p>Have you had a recent A1C level test? What was it?</p> <p>Have you had any complications from your diabetes?</p> <p>Do you have any heart or kidney issues?</p>
Medication knowledge	<p>Tell me about the medications you use to manage your diabetes.</p> <p>Which medications do you currently take, and why do you take each medication?</p>
Medication adherence	<p>How difficult is it for you to remember to take your medications?</p> <p>How often do you miss a dose of your diabetes medication?</p>
Medication concerns	<p>What worries you most about your diabetes medications?</p> <p>Have you had any issues with low blood sugar in the past?</p>
Healthy lifestyle/weight management	<p>Please describe your diet and regular physical activity routines.</p> <p>How concerned are you about weight gain from your diabetes medications?</p>
Patient preferences	<p>What type of medications do you prefer (eg, route of administration and frequency of administration)?</p>

By gathering information from patients, pharmacists can identify patients who may be ideal candidates for a GLP-1 receptor agonist, based on patient-specific factors and preferences.⁶ For example, a GLP-1 receptor agonist is an add-on option to metformin for patients in which weight gain is a concern or for those who need to minimize the risk of hypoglycemia. If a GLP-1 receptor agonist is appropriate, pharmacists can query patients about their medication preferences such as route of administration, preferred dosing frequency, etc. Assessing and addressing barriers to medication adherence is also essential for improving long-term outcomes.⁷

Once prescribed a GLP-1 receptor agonist, patients should be educated on appropriate administration and timing of doses, proper storage, and potential adverse events. The impact on blood glucose, A1C, and weight should also be discussed. Appropriate administration sites for subcutaneous injections and proper administration technique should also be reviewed with patients. Many websites have videos on proper device use

and patients should be directed toward these sites for additional demonstrations on appropriate use. Patients should be aware of common and more serious adverse events that may occur and educated on ways to help mitigate some of these effects. Educating patients to be mindful of portion sizes may help to reduce the risk of nausea and other GI effects.⁶

GLP-1 analogs are contraindicated in patients with a personal or family history of medullary thyroid cancer (MTC) and in patients with multiple endocrine neoplasia syndrome type 2 (MEN2). Additionally, GLP-1 analogs are associated with the development of acute pancreatitis. Patients should be monitored for signs or symptoms of acute pancreatitis. Additionally, GLP-1 analogs may be contraindicated in patients with a history of acute pancreatitis. Other common adverse effects associated with GLP-1 analog use include gastrointestinal symptoms, such as nausea, vomiting or diarrhea, as well as injection site reactions.



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Case study

BF is a 60-year-old white male with type 2 diabetes. He reports that all of his blood glucose values are “in the 180s” and he is not happy with these numbers. His personal A1C goal is <7%. BF has a past medical history of hypertension for 8 years, type 2 diabetes for 2 years, dyslipidemia for 6 years, and established ASCVD. He is also overweight per his body-mass index (BMI) (28.4). His last A1C value 6 months ago was 8.1% and his only antihyperglycemic agent is metformin 1000 mg taken twice daily which was started when he was diagnosed about two years ago. BF is concerned about his weight and states that he would like a medication that will not make him gain weight. He has been happy with his metformin therapy citing he has experienced minimal side effects with this medication.

BF is in need of additional add-on therapy to his metformin because he is not at his A1C goal and his glucose levels have been elevated. A GLP-1 receptor agonist with proven CVD benefit, defined as a label indication for reducing CVD events, would be a good option for him because of his established ASCVD. The effect of GLP-1 receptor agonists on weight also is a consideration for BF. Education regarding timing, administration, storage, and side effects are important points to cover. The impact on blood glucose, A1C, and weight should also be discussed with BF.

RESOURCES FOR SUPPORTING PATIENTS WITH DIABETES

APhA Pharmacist and Patient-Centered Diabetes Care Certificate Training Program

An educational experience designed to equip pharmacists with the knowledge, skills, and confidence needed to provide effective, evidence-based diabetes care.

www.pharmacist.com/education/pharmacist-patient-centered-diabetes-care

Centers for Disease Control (CDC) National Diabetes Education Program

Provides culturally and linguistically appropriate diabetes education resources for a range of individuals and groups.

www.cdc.gov/diabetes/ndep/index.html

Association of Diabetes Care and Education Specialists

An organization dedicated to improving prediabetes, diabetes and cardiometabolic care through innovative education, management, and support.

www.diabeteseducator.org/about-adces

American Diabetes Association

An organization dedicated to the prevention and cure of diabetes with a multitude of patient-friendly resources available on their website.

www.diabetes.org/about-us



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