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Saudi Consensus for Oral Semaglutide, the Recent Innovation in GLP-1 RAs Era; Consensus Report

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Abstract

GLP-1 receptor agonists (GLP-1 RAs) are among the most successful medications for treating people with type 2 diabetes mellitus (T2DM), giving reasonable glycemic control with a low risk of hypoglycemia in those who have failed to control their condition with other oral anti-diabetic drugs (OADs). However, GLP-1RAs are underutilized—as time patients remained on their last oral treatment regimen with inadequate glycemic control prior to GLP-1RA initiation is on average of 19 month—despite evidence supporting their effectiveness, safety, and possible CV outcome advantages. With the new advances in GLP-1 RAs, the first oral form for the semaglutide molecule was developed with proven efficacy, safety, and patient preferences that may help pave the road for more utilization of this class. Therefore, we, a Saudi task force, gathered to develop an explicit, evidence-based consensus on oral semaglutide use in Saudi patients with diabetes. The panel recommends a GLP-1RA in those T2DM patients with or without or at high risk for ASCVD, HF, and/or CKD when there is a need to minimize weight gain or promote weight loss, or when there is a need to minimize hypoglycemia. Ensure that people

with T2DM and ASCVD, HF, or CKD are treated appropriately with an SGLT-2i or GLP-1 RA. This approach should be initiated independent of background therapy, glycaemic control, or individualized treatment goals. Healthcare professionals should do their best to prevent clinical inertia in T2DM to help people with T2DM achieve better glycemic control and prevent or delay diabetes-related complications. The availability of oral forms of GLP-1RA medications could help combat this problem of clinical inertia to start GLP-1RA at the right time, as patients prefer oral to injectable forms. The availability of oral GLP-1RA can help in starting this class early and encourage healthcare professionals in prescribing it at the right time. Moreover, it can help those patients who fear of the injections. The panel recommends the oral GLP-1RA semaglutide to be used early and encourage healthcare professionals in prescribing it at the right time. The injectable form can be preserved for further intensification of therapy whenever needed as add-on therapy particulary for poly-medicated patients for better compliance at this stage.

Keywords

Glucagon-Like Peptide-1 Receptor Agonists, T2DM, Glycemic Control, Semaglutide, Oral Semaglutide, Injectable Semaglutide

1. Introduction

According to the data of the International Diabetes Federation (IDF) Diabetes Atlas, the prevalence of diabetes mellitus (DM) worldwide is expected to be above 9.5% by the year 2040, with a total number of more than six hundred Million [1]. In addition, the prevalence of DM is escalating rapidly in the Kingdom of Saudi Arabia (KSA) with an average number of 4.3 million, accompanied by the consequent over-exhaustion of the resources related to the healthcare system [2].

Diabetes is linked to several debilitating long-term consequences that considerably impact patient quality of life (QOL) and lead to significant morbidity, mortality, and healthcare resource use [3] [4] [5]. As a result, D.M. was ranked as the 15th leading cause of life-years lost in 2015 [6].

In persons with type 2 diabetes mellitus (T2DM), poorly managed glycemia and delayed treatment intensification increase the risk of microvascular complications and cardiovascular (CV) disease [7] [8]. In one study in KSA (2020), just 65% of persons with T2DM did not meet their glycated hemoglobin (HbA1c) objective [9]. As a result, despite the numerous therapies available, a significant segment of the T2D population is at greater risk of diabetes-related complications.

GLP-1 receptor agonists (GLP-1 RAs) are among the most successful medications for treating people with T2D, giving reasonable glycemic control with a low risk of hypoglycemia in those who have failed to control their condition

with other oral anti-diabetic drugs (OADs), such as metformin [10] [11]. GLP-1 is a hormone produced by the intestines that stimulates insulin production and reduces glucagon production, which helps lower blood sugar levels. GLP-1RAs mimic the effects of GLP-1 by binding to and activating the GLP-1 receptor on the surface of pancreatic cells, leading to increased insulin secretion and decreased glucagon secretion [12]. Many GLP-1 RAs are available such as Exenatide, Liraglutide, Dulaglutide, Albiglutide, Semaglutide and Lixisenatide [13] [14].

GLP-1RAs are underutilized—as time patients remained on their last oral treatment regimen with inadequate glycemic control prior to GLP-1RA initiation is on average of 19 month—despite evidence supporting their effectiveness, safety, and possible CV outcome advantages [15] [16].

With the new advances in GLP-1 RAs, the first oral form for the semaglutide molecule was developed and approved by The U.S. Food and Drug Administration in 2019, with proven efficacy, safety, and patient preferences that may help pave the road for more utilization of this class [17].

Therefore, we, a Saudi task force (endocrinologists, diabetologists and internal medicine experts), gathered to develop an explicit, evidence-based consensus on oral semaglutide use in Saudi patients with diabetes, when, why, and how? This article has the recommendations of this expert panel.

2. Value versus Underutilisation of GLP-1 RA: Insights from the Latest Evidence

2.1. Role in Management of T2DM According to Recent Guidelines

In 2005, the US Food and Drug Administration (FDA) approved exenatide (the first GLP-1RA) initially. Since that time, agents of the GLP-1RA class of drugs have swiftly acquired interest as an option for the management of hyperglycemia in T2DM. This was attributed, at least in part, to their clinical effectiveness in improving glycemic control and weight loss in persons with T2DM [18] [19] [20].

GLP-1RA with proven CVD benefit with or without metformin based on glycemic needs, are appropriate initial therapy for individuals with T2DM with or at high risk for atherosclerotic cardiovascular disease (ASCVD), HF, and/or chronic kidney disease (CKD) [21]. The recent 2022 ADA guideline adopted a multifactorial approach to the reduction in risk of DM complications. In patients with T2DM and established ASCVD or multiple risk factors for ASCVD, a GLP-1 RA with demonstrated CV benefit is recommended to reduce the risk of major adverse cardiovascular events (MACE) [22]. The EASD/ADA consensus report and the European Society of Cardiology guidelines state that, independent of the target HbA1c, people with T2D and atherosclerotic CVD or CKD should preferentially receive a GLP-1RA with proven benefit in reducing cardiovascular risk and/or CKD progression [23]. Moreover, combined therapy with sodium-glucose co-transporter-2 inhibitor (SGLT-2i) with demonstrated CV benefit and

a GLP-1 RA with demonstrated CV benefit may be considered for an additive reduction in the risk of adverse CV and kidney events [24]. A GLP-1 RA with good weight loss efficacy is preferred for people who do not have ASCVD, HF, and/or CKD or who are not at high risk for developing these conditions when there is a need to minimize weight gain or promote weight loss. A GLP-1 RA is also advised when it is necessary to reduce hypoglycemia [25].

Also, the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE), in their consensus statement in 2020, recommended that for patients with T2DM, independent of glycemic control, GLP-1 RA and SGLT-2i with proven ASCVD and/or CKD benefits may be preferred in patients with those complications [25]. Finally, the 2021 European Society of Cardiology (ESC) guideline, in persons with T2DM and ASCVD, the use of a GLP-1 RA or SGLT-2i with proven outcome benefits is recommended to reduce CV and/or cardiorenal outcomes (class of recommendation I & evidence A). The view of the ESC is that metformin should be considered but is not mandatory first-line treatment in patients with ASCVD or evidence of target organ damage (TOD). Also, the initiation of metformin in such patients should not forego or delay the initiation of evidence-based SGLT-2i or GLP-1 RA [26].

Panel Recommendation 1

We recommend a GLP-1RA in those T2DM patients with or without or at high risk for ASCVD, HF, and/or CKD when there is a need to minimize weight gain or promote weight loss, or when there is a need to minimize hypoglycemia.

Panel Recommendation 2

Ensure that people with T2DM and ASCVD, HF, or CKD are treated appropriately with an SGLT-2i or GLP-1 RA. This approach should be initiated independent of background therapy, glycaemic control, or individualized treatment goals.

2.2. Underutilization in T2DM Management

In the CAPTURE study, a multinational, cross-sectional study of CVD prevalence in adults with T2DM across 13 countries, including the KSA, despite guideline recommendations, only 2/10 (21.5%) people with T2DM having CVD are getting a glucose-lowering treatment with proven CV benefit. Thus, there is underutilization of GLAR-1RA and SGLT-2i in that category of patients [27].

In a medical record review conducted in the UK via a physician survey, the authors examined time to treatment intensification with GLP-1 RAs. The median time from T2DM diagnosis to GLP-1 RA initiation was 6.1 years (mean ± SD: 7.8 ± 6.9 years). Patients treated by general practitioners (GPs) had a significantly longer duration of time with insufficient glycaemic control prior to GLP-1 RA initiation compared with patients treated by diabetes specialists (median time for specialists was 11.0 months vs. 17.0 months for GPs; $p = 0.038$). The study's findings revealed that medication intensification is frequently delayed, despite consistently poor glycemic control for more than 12 months, contrary to

treatment guidelines. According to the findings of this study, some T2DM patients may benefit from more rapid treatment intensification, which could improve glycemic control and lower the risk of a variety of short- and long-term health consequences [16].

According to several studies, patients and doctors may hesitate to start these injectable treatments (GLP-1RA) despite their potential health benefits [16] [28] [29] [30]. Clinical inertia is used to designate a patient's unwillingness to start or intensify medication. It can have substantial consequences, including an increased risk of poor glycemic control and various diabetes-related problems [16].

A large corpus of research has looked into clinician complacency and patient resistance to starting injectable treatment like insulin. Clinicians, for example, may be hesitant to prescribe insulin because of fears of patient noncompliance, hypoglycemia, and the notion that patients will not want to utilize injections [31]-[37].

Patients have also expressed apprehension about starting injectable treatment like insulin because they are afraid of injections and hypoglycemia and are concerned about potential lifestyle constraints and weight increase [38]. In addition, research including large groups of patients has looked at the duration of delays in insulin treatment intensification [38].

Despite the failure to achieve the goal of HbA1c, treatment intensification was frequently prolonged by over a year, according to a systematic review of five of these studies [39]. According to a physician survey, injectable GLP-1 RAs may have a similar level of inertia [40].

When oral or insulin therapy alone does not provide adequate glycemic control for T2DM patients, this class of treatment is frequently indicated as an addition to a treatment plan [16]. Despite the efficacy of GLP-1 RA for glycemic control and potential weight reduction advantages [16], a physician survey revealed reasons for clinical inertia. These reasons are being not considered first line therapy according to guidelines at the time of the survey (56.9%) and being injectable administration (44.6%) [40].

Several concerns, like GLP-1RAs not being the recommended first-line therapy according to treatment recommendations, the injectable form of administration, the expense, and the possibility of gastrointestinal adverse effects, caused clinicians to hesitate when prescribing this class. In addition, about a quarter of GPs said they lacked the knowledge to prescribe a GLP-1 RA [16].

Also, in the KSA, about a third (34.6 percent) of participants with T2DM were unwilling to start using injectable therapy like insulin. Participants most frequently expressed the following negative attitudes toward starting insulin therapy: using insulin only as a last resort (57.1%), restricting one's lifestyle (48.8%), and problematic hypoglycemia (45.1%), and perception of previous failure to care for diabetes (44.6%), and weight gain concerns (44.6%) (40.7 percent) [41].

For some people, the requirement to deliver GLP-1RA through subcutaneous

injection is a practical constraint. For individuals who are hesitant or unable to start a GLP-1RA for this reason, an oral formulation of semaglutide, which is currently licensed for the treatment of T2DM, is available [42].

While perceived high acquisition costs and positioning in clinical guidelines are factors, apprehension about using subcutaneous injectable medications may also play a role, with up to 49% of general practitioners in the UK reporting that the injectable route of administration is a barrier to prescribing a GLP-1 RA [40]. There is also the time and resources spent by healthcare workers educating people with T2DM about starting injectable therapies [43].

In a local two-arm study surveying 700 patients and 400 physicians all over the entire regions of KSA, it was evident that the most frequent reason behind hesitance to prescribe (physician response) or use (patients' response) GLP-1RA on the right time according to the international guidelines is being injectable [44].

Panel Recommendation 3

Healthcare professionals should do their best to prevent clinical inertia in T2DM to help people with T2DM achieve better glycemic control and prevent or delay diabetes-related complications.

The availability of oral forms of GLP-1RA medications could help combat this problem of clinical inertia to start GLP-1RA at the right time, as patients prefer oral to inectable forms.

3. Early Initiation with GLP-1RA

People with T2DM have a sizable unmet need in this area. CVD ranks as the leading cause of disability and mortality for those persons. According to a 2018 comprehensive assessment of scientific evidence from around the world, 32.2 percent of people with T2DM experience CVD. It accounts for over half of all fatalities during the research period, making it a substantial cause of mortality among persons with T2DM. The leading causes were coronary artery disease and stroke. Additional modifiable risk factors include excess body weight, dyslipidemia, hypertension, and inactivity affect more than 80% of patients with T2DM. Less than 30% of patients meet their ABC (blood pressure, cholesterol, and HBA1c) treatment goals for controllable risk factors [45] [46] [47] [48].

Early and efficient glycaemic management is linked to lower risks of microvascular and macrovascular complications, according to the Diabetes and Aging Study (2019). HbA1c levels of more than 6.5% one year after diagnosis were linked to worse outcomes among individuals with newly diagnosed T2DM and ten years of survival. New patients may require prompt, intense therapy to prevent an unrecoverable long-term risk for diabetic complications and mortality [49].

Uncontrolled blood sugar is linked to a significant burden of CVD and death. One year of clinical inertia could add 7%, 8%, and 18% to the cumulative occurrences of retinopathy, neuropathy, and nephropathy over 25 years. Stroke, myo-

cardial infarction, and CV death increased by 8%, 8%, and 15%. Clinical inertia may have severe consequences on populations that delay therapy for a more extended period, are over 65, or are non-Hispanic whites. Clinical inertia based on HbA1c readings every three months, in this case, determines whether the patient requires treatment intensification [50].

Boye *et al.* (2020) also looked into the connection between the timing of GLP-1RA initiation and HbA1c readings among T2DM patients. The authors demonstrated that starting GLP-1RA earlier was linked to more significant decreases in HbA1c. Over two years, starting a GLP-1 RA was linked to a 0.6 percent decline in HbA1c levels ($p < 0.0001$). Early initiation had the highest odds of obtaining a post-period HbA1c level of 7% (odds ratio, 4.9; 95% CI, 3.0 - 8.1) and a reduction in HbA1c levels of 1.3 percent ($p < 0.0001$). The findings show that although starting a GLP-1RA is typically linked to lower HbA1c levels, starting a GLP-1RA earlier may have additional therapeutic advantages [51].

It is crucial to address the cardiometabolic risk factors sooner in the ASCVD continuum. Therefore, early multifactorial therapy is required to lower the risk of problems in T2DM patients [52] [53]. Improvements in glucose metabolism, weight loss, blood pressure reduction, improved lipid profiles, and a decrease in inflammation are all advantages of GLP-1RAs in ASCVD. Progress may be slowed down or stopped with early intervention [54] [55].

Panel Recommendation 4

It might be necessary for medical practitioners to alter the T2DM trajectory so that GLP-1RA can be started as soon as appropriate. The earlier treatment begins, the better the impact on glucose control and the ability to prevent or postpone problems associated with diabetes.

4. The First Oral GLP-1RA Agent: Oral Semaglutide the Latest Innovations in This Scope

Semaglutide is a human GLP-1 analogue having 94% homology to human GLP-1 [56]. Semaglutide is available in two formulations. Oral semaglutide is suitable for once-daily dosing. Subcutaneous semaglutide is suitable for once-weekly dosing. The same semaglutide molecule is present in both formulations, with the same mode of action and effects. The same pharmacological effect is achieved with once-daily dosing of oral semaglutide as with once-weekly subcutaneous semaglutide [56].

Similar exposure-response relationships were observed for efficacy and tolerability of semaglutide, regardless of the route of administration, indicating that more significant variability in plasma concentration levels for oral semaglutide does not impact response. Exposure-response analyses showed greater HbA1c and body weight reductions, and more GI side effects, with increasing semaglutide exposure. The route of administration does not affect the efficacy and safety of semaglutide, according to the analyzed population data from the SUSTAIN and PIONEER trials. This analysis indicates that the route of administration does not affect the efficacy and safety of semaglutide [57].

Despite early and efficient glycemic management advantages in T2DM, some patients have difficulty meeting HbA1c goals. The only GLP-1RA that is offered in both an injectable and oral formulation is semaglutide. In the global SUSTAIN and PIONEER phase III clinical trial programs, the effectiveness of once-weekly subcutaneous semaglutide and once-daily oral semaglutide has been examined in a variety of clinical settings, including early T2DM managed with diet and exercise only, established T2DM uncontrolled on one to three oral antidiabetic drugs, and advanced disease treated with insulin [58].

Across the SUSTAIN program, compared to sitagliptin, liraglutide, exenatide extended-release, dulaglutide, canagliflozin, or insulin glargine, once-weekly subcutaneous semaglutide 1.0 mg lowered HbA1c by 1.5 - 1.8 percent after 30 - 56 weeks [58].

After 26 weeks, once-daily oral semaglutide 14 mg decreased HbA1c by 1.0 - 1.4 percent across the PIONEER program, significantly more than other OADs like sitagliptin or empagliflozin and to a similar degree as liraglutide. Additionally, oral semaglutide lowered body weight more than sitagliptin and liraglutide and to a similar level as empagliflozin. In contrast, subcutaneous semaglutide reduced body weight much more than all active comparators examined [58].

There is no evidence linking any semaglutide formulation to a higher risk of hypoglycemia. Both oral and injectable forms of semaglutide provide the advantage of a highly effective GLP-1RA. To better meet the needs and preferences of the patient, the optimal formulation can be chosen on an individual basis [58].

In the PIONEER3 trial, oral semaglutide significantly improved HbA1c reduction (−1.3%) vs. sitagliptin (−0.8%). Also, it significantly reduced body weight (−3.1 kg) vs. sitagliptin (−0.6%). A significantly more significant proportion (44.7%) achieved composite endpoint vs. sitagliptin (20.2%) [59].

Also, it significantly improved HbA1c reduction (−1.3%) vs. empagliflozin (−0.9%), similar weight reduction (−3.8 kg) vs. empagliflozin (−3.7 kg). A significantly greater proportion (60.5%) achieved composite endpoint vs. empagliflozin (35.7%) in the PIONEER 2 trial [60]. Moreover, oral semaglutide improves blood lipids and reduces systolic blood pressure. Each ten mmHg decrease in mean systolic blood pressure is associated with reductions in ASCVD risk in people with T2DM [61]. In addition, it reduced inflammation marker high-sensitivity C-reactive protein (hsCRP) levels vs. comparators like empagliflozin or placebo [62]. Energy intake and food consumption are reduced with semaglutide vs. placebo [63]. Semaglutide also reduced waist circumference, an independent predictor of atherosclerotic CVD risk, at 26 weeks [59] [60] [64].

SUSTAIN-6 and PIONEER-6 were two CVOTs that investigated the effect of semaglutide on MACE. In SUSTAIN-6, 26% MACE risk reduction confirms CV safety and superiority of semaglutide vs. placebo PIONEER-6 Event-driven. 21% MACE risk reduction confirms CV safety and non-inferiority of semaglutide vs. placebo [61] [65]. Semaglutide reduced the time to the first occurrence of MACE compared with placebo in dedicated CVOTs [66].

Practically, oral semaglutide is taken once daily and should be taken in a fast-

ing state. Available in 3, 7, and 14 mg doses. The dose is escalated every four weeks from the starting dose of 3 mg to mitigate GI AEs. No dose adjustment of oral semaglutide is required in special populations like patients with mild, moderate, or severe renal impairment, patients with hepatic impairment, and elderly patients [67].

Panel Recommendation 5

The availability of oral GLP-1RA can help in starting this class early and encourage healthcare professionals in prescribing it at the right time. Moreover, it can help those patients who fear of the injections.

5. Changing the Trajectory of T2DM with Real-World Insights on Early Use of Oral Semaglutide

As RCTs did not tell us how oral semaglutide is used in clinical practice, the IGNITE study was designed to evaluate the first patterns of routine clinical use of oral semaglutide and assess patients' clinical characteristics and glycaemic control in the real world [68].

The IGNITE study is a retrospective, observational cohort study that presented early data on the use of oral semaglutide in clinical practice from the US IBM Explorys electronic health record database. It included 782 patients prescribed oral semaglutide, 54.5% were women, and the mean age (SD) was 57.8 years (11.3); 66.0% of patients received their prescription from a primary care practitioner. They have had a high rate of obesity, other comorbidities, and diverse treatment backgrounds. Results indicated that HbA1c reductions up to −2.1% were observed, even though 26.1% of this cohort did not have a dose escalation beyond the initial 3 mg dose. About a third of patients had the highest prescribed dose of 3 mg; perhaps therapeutic inertia and potential tolerability issues prevented dose escalation. These data highlight an opportunity to fully bridge existing treatment and education gaps to realize the potential of oral GLP-1RA therapy fully [68].

The average HbA1c of the Saudi DM population is sub-optimal, as indicated by data from the Saudi National Diabetes Registry gathered from 22 Health Institutes in KSA encompassing more than 84,000 patients. Therefore, oral semaglutide provides clinicians with opportunities to individualize treatment in patients with T2DM and can be used to address several treatment considerations or common comorbidities in those patients [23] [69].

6. Could We Use Oral GLP-1RA and Injectable GLP-1RA in the Same Formulary?

Convenience and hatred of needles were the two most common arguments for choosing tablets. 76.5% of T2DM patients prefer a once-daily oral vs. once-weekly injectable medication. Adherence to injectable regimens is lower than to oral drugs [70] [71] [72] [73].

Most people with T2DM is treated by primary care—approx. 90%. Treatment

regimens are becoming increasingly complicated, and the amount of time per patient is decreasing, resulting in more complicated management. Diabetes management has become increasingly complex because of multiple medication categories (including combination medicines), the need to avoid hyper- and hypoglycemia, multiple options of medical devices, need to facilitate patients' lifestyle changes [74].

Early oral semaglutide therapy improves patient health now and in the long term. Crossing the Injection Frontier is an emotional obstacle for patients, perceived as a point of no return. Oral semaglutide allows the benefits of semaglutide early before crossing the injection frontier [74].

Panel Recommendation 6

The panel recommends the oral GLP-1RA semaglutide to be used early and encourage healthcare professionals in prescribing it at the right time.

The injectable form can be preserved for further intensification of therapy whenever needed as add-on therapyparticulary for poly-medicated patients for better compliance at this stage.

7. Cost-Effectiveness of Oral Semaglutide

Examining the costs and health effects of one or more interventions is possible through the process of cost-effectiveness analysis (CEA). By evaluating how much it costs to obtain a unit of a health outcome, like a life year gained or a death prevented, it compares an intervention to another intervention (or the status quo) [75].

Oral semaglutide represents good clinical and economic value for patients with T2DM. The OFFSET research looked at the financial effects of treating individuals with T2DM and CVD with GLP-1 RAs (n = 1712) as opposed to standard therapy (n = 122,334). These individuals can be given a GLP-1RA as first line medication or as an addition to metformin, according to the 2019 changes to the ESC and ADA/EASD guidelines. This strategy, nevertheless, has financial ramifications. The purpose of this study, according to the authors, was to compare the expenditures of healthcare for patients receiving GLP-1RA therapy versus normal treatment. According to the study, lower inpatient and outpatient care expenses balance the extra medical cost of GLP-1RA medication in patients with T2DM and a CVD-related hospitalisation, resulting in budget neutrality compared to standard of care [75].

Another study compared oral semaglutide to empagliflozin, sitagliptin, and liraglutide in the UK based on the PIONEER Program to see which was more long-term cost-effective. In comparison to empagliflozin, sitagliptin, and liraglutide, oral semaglutide increased quality-adjusted life expectancy by 0.09, 0.20, and 0.07 quality-adjusted life years, respectively. Direct expenses during a patient's lifetime were GBP 1551 less with oral semaglutide than with liraglutide, but GBP 971 and GBP 963 higher than with empagliflozin and sitagliptin, respectively. Compared to all comparators, oral semaglutide was linked to a lower

incidence of diabetes-related complications. Therefore, compared to empagliflozin 25 mg and sitagliptin 100 mg, oral semaglutide 14 mg was associated with incremental cost-effectiveness ratios of GBP 11,006 and 4930 per QALY gained, respectively, and was more efficient and less expensive (dominant) than liraglutide 1.8 mg. The authors came to the conclusion that oral semaglutide was more cost-effective than empagliflozin, sitagliptin, and liraglutide for the treatment of type 2 diabetes. Cost-effectiveness improvements were driven by benefits in glycaemic control and BMI, leading to a reduced incidence of diabetes-related complications and an improved quality of life [76].

8. Conclusion

With the availability of the oral form of the GLP-1RA semaglutide, the expert panel recommends using this oral form early in T2DM cases and preserving injectable form of GLP-1RA to be added on therapy when further intensification of treatment is needed.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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