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SEMAGLUTIDE- Injectable therapy for T2DM

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Abstract:
People with type 2 diabetes (T2D) who require treatment intensification, injectable treatments such as glucagon-like peptide-1 receptor agonists (GLP-1RAs) and insulin are high-efficacy choices. GLP-1RAs offer weight loss benefits in addition to high glycemic effectiveness, and several agents have been proven to lower cardiovascular risk. The fact that semaglutide is a glucagon-like peptide-1 (GLP-1) hormone with substantial effects on glycemic control and body weight regulation has prompted efforts to increase its half-life and make it therapeutically beneficial in persons with type 2 diabetes (T2D).
Key words*: diabetes mellitus, glucagon like peptide -1 receptor agonists, semaglutide*

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I. Introduction:

Drug: Semaglutide is a glucagon-like peptide-1 (GLP-1) hormone with substantial effects on glycemic control and body weight regulation has prompted efforts to increase its half-life and make it therapeutically beneficial in persons with type 2 diabetes (T2D).

Indication: Semaglutide is indicated for the once-weekly treatment of adult patients with type 2 diabetes mellitus to improve glycemic control, in combination with:

- Diet and exercise in people who cannot take metformin because of a contraindication or intolerance. When diet and exercise, as well as the maximum tolerable dose of metformin, are insufficient to achieve appropriate glycemic control, metformin is used.
- When diet and exercise, as well as dual therapy with metformin and a sulfonylurea, do not provide optimal glycemic control, metformin and a sulfonylurea are used. When nutrition and exercise are combined with basal insulin and metformin, the result is basal insulin with metformin.
- Semaglutide is not a substitute for insulin. Semaglutide should not be used in patients with Type 1 diabetes mellitus (formerly known as insulin-dependent diabetes mellitus or IDDM) or for the treatment of diabetic ketoacidosis.

Mechanism of Action:

Semaglutide is a GLP-1 receptor agonist that binds and activates the GLP-1 receptor selectively. Native GLP-1, an endogenous incretin hormone that potentiates glucose-dependent insulin production from pancreatic beta cells, binds to the GLP-1 receptor. Semaglutide, unlike native GLP-1, has a pharmacokinetic profile in humans that makes it acceptable for once-weekly administration. Following subcutaneous administration, the delayed action profile is based on albumin binding, which lowers renal clearance and increases enzymatic stability towards the dipeptidyl peptidase (DPPIV) enzyme, resulting in a one-week plasma half-life. The action of semaglutide is mediated by a particular interaction with GLP-1 receptors, which results in a rise in cyclic adenosine monophosphate levels (cAMP). Insulin secretion is stimulated by semaglutide in a glucose-dependent manner. Glucagon secretion is also reduced by semaglutide in a glucose-dependent manner. Insulin secretion is enhanced and glucagon secretion is suppressed when blood glucose levels are high. Semaglutide, on the other hand, reduces insulin secretion while having no effect on glucagon secretion when blood glucose levels are low. [1] .

II. Discussion:

T2DM is a long-term, progressive illness marked by persistent hyperglycemia. GLP-1 RAs can help people lose weight, which is especially advantageous for T2DM patients who also have obesity[3] In T2DM, semaglutide is typically administered as a supplement to diet and exercise. When compared to alternative medications, previous studies shown that patients with T2DM who were treated with semaglutide had a significant reduction in HbA1c percent and body weight [4] When compared to other GLP-1 RAs, semaglutide

exhibited a considerable improvement in glycemia and bodyweight control. Semaglutide is superior to other once-weekly administered GLP-1 RAs (exenatide extended release and dulaglutide) in terms of not just glycemia control but also body weight control and other efficacy statistics, according to recent head-to-head studies [3,5] t's yet unclear whether semaglutide is more effective and has fewer side effects. Furthermore, no relevant systematic review has been published to far. The goal of this study is to see how effective and safe semaglutide is in T2DM patients. We'll look at the effect of efficacy and safety in different semaglutide dosages, different controls, and different follow-up periods. We will present a complete picture of semaglutide in terms of efficacy and safety. Different authors will check articles at least three times each to confirm the correctness and reliability of the results. meta-analysis will be based on enough evidence to ensure its trustworthiness. This systematic review will be to assess the efficacy and safety of semaglutide in T2DM patients, potentially providing an objective and thorough understanding of the drug. [3,5]

Dose and Dosage form:

Semaglutide is a once-weekly subcutaneous injection available as a prefilled pen. It should be stored in a refrigerator until first use but then may be kept at room temperature for up to 56 days. The recommended starting dosage is 0.25 mg once weekly for four weeks, then increased to 0.5 mg once weekly. If additional glycemic control is needed, the dosage should be increased to 1.0 mg once weekly.

Safety:

Semaglutide was well tolerated and demonstrated a safety profile similar to other GLP-1RAs (6,7). The most frequent adverse events with semaglutide were gastrointestinal; these were mainly mild or moderate and generally decreased in frequency over time. Nausea was the most common adverse event observed with semaglutide. Severe or blood glucose-confirmed symptomatic hypoglycemia events were fewer or similar with semaglutide vs comparators, irrespective of background OAD treatment. No unexpected safety issues were identified (8–10)

Adverse Drug Reaction

The most frequently reported adverse reactions in clinical trials were gastrointestinal disorders, including nausea, diarrhoea and vomiting. In general, these reactions were mild or moderate in severity. More patients taking semiglutide versus comparator drugs had severe or serious adverse events and/or discontinued treatment due to gastrointestinal disorders. The following serious adverse reactions are described:

- Risk of Thyroid C-cell Tumors
- Pancreatitis
- Diabetic Retinopathy Complications
- Use with Medications Known to Cause Hypoglycaemia
- Renal Insufficiency

Abbreviations:
type 2 diabetes (T2D)
glucagon-like peptide-1 receptor agonists (GLP-1RAs)
cyclic adenosine monophosphate (cAMP)
dipeptidyl peptidase (DPPIV)

Reference:

[1]. OZEMPIC® (semaglutide injection) Product Monograph
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