

Let's Lower  
**#WeightofDiabetes**  
with

FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES

**RYBELSUS**®

semaglutide tablets

A GAME CHANGER. A LIFE CHANGER.



**OBJECTION**

H A N D L E R

# OBJECTION

## H A N D L E R

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## Framework for objection handling

<b>Support</b>	the HCP's concern
<b>Obtain</b>	the reason for the concern
<b>Listen</b>	to the reason in full
<b>Validate</b>	your understanding of the issue
<b>Explain</b>	how you can SOLVE the concern

**Doctor:** Hi good morning/ evening there are some media reports today that use of GLP-1 RA has some safety concerns in people with type 2 diabetes.

### **Support, do not react to HCPs concern:**

Dear doctor thank you so much for sharing your concerns with me.

### **Obtain the reason for concern:**

Doctor may I request you to be please elaborate about the concerns you may have with the usage of GLP-1 RA in T2DM.

**Doctor:** Yes indeed, media report suggests that there may be increased risk of thyroid cancer with usage of GLP-1 RAs in people with type 2 diabetes.

### **Listen to the concern attentively:**

Pay close attention to the HCP's tone of voice and body language to better understand them. Offer short comments such as "This is a serious concern" or "I understand your concern" to help the HCP feel comfortable sharing.

### **Validate your understanding of the issue:**

I truly appreciate your concern, if I understand you right, you mean that there may be an increased risk of thyroid cancer with the use of GLP-1 RAs in people with type 2 diabetes.

### **Explain with facts and empathy:**

Allow me to present some facts and our responsibility toward the patient safety.

EVIDENCE as mentioned in subsequent pages.

## Framework for objection handling

### For all safety concerns:

- Patient safety has top priority for Novo Nordisk, and we take all reports about adverse events from use of our medicines very seriously.
- GLP-1RAs have been used to treat type 2 diabetes for more than 15 years and for treatment of obesity for 8 years, including Novo Nordisk products based on semaglutide and liraglutide that have been on the market for more than 10 years.
- We have over 9.5 million total patient-years of experience on Semaglutide across RCTs and RWEs.
- Novo Nordisk remains confident in the benefit risk profile of the products and remains committed to ensuring patient safety

### Summary : Summarize as mentioned in subsequent pages

*Dear Sir/madam hope I could address your concerns please let me know if you need any further details on the same.*

*Thank you so much for your insightful discussion and understanding. I Look-forward for your kind support.*



## Thyroid Problem: Medullary Thyroid Cancer

- Across the safety trials of all GLP-1RAs and the meta-analysis of existing studies has shown that there is no increased risk of thyroid cancers with GLP-1RA usage<sup>1,2,3&4</sup>
- The risk of GLP-1RAs and medullary thyroid cancer has been linked only in animal studies.
- The expression of GLP-1 receptors in human thyroid tissue is not as high as rodents hence the link for the risk of MTC in humans has not established yet<sup>6</sup>
- An Ongoing MTC Surveillance Registry has been developed to address any association between medullary thyroid carcinoma and GLP-1 RA usage. it is a joint sponsored cancer registry running since 2010 based on us cancer registry<sup>7</sup>

### Evidence<sup>1-14</sup>

- The LEADER CVOT trial investigated the long-term effects of liraglutide on the thyroid and markers of thyroid function and showed no difference in calcitonin levels over time between liraglutide and placebo treated subjects and no cases of medullary thyroid carcinoma were seen with liraglutide (1 case in the placebo group).
- In a review of the SUSTAIN 1-7 trials including over 8000 patients across the spectrum of T2D, the low incidence of malignant neoplasms was similar between comparators and subcutaneous semaglutide.
- A similar review of the PIONEER 1-10 trials in over 9000 patients revealed that the number of malignant neoplasms reported were few with no clustering of events in any particular system organ or class.
- Recently Hu et al., performed a large-scale meta-analysis which included over 50,000 patients to evaluate the occurrence of thyroid disorders with GLP-1RA treatment. In line with previous reporting, GLP-1RA had no significant effects on the occurrence of thyroid cancer.

*To summarise Dear sir/madam to date, the Novo Nordisk assessment of safety data collected from large clinical trial programs, post-marketing surveillance and other relevant sources of information have not shown a causal relationship between semaglutide (or liraglutide) and thyroid cancer.*



## Eye Problem: Retinopathy

- Among safety trials conducted for the different GLP-1RAs, the results are inconsistent as one shows increased risk others show either protective effect or no difference to placebo<sup>8</sup>
- This increased risk noticed is also referred as early worsening of diabetic retinopathy which is due to intensive glycemic control and seen in various anti-diabetic therapies, bariatric surgery and pregnancy<sup>9,10</sup>
- This early worsening is not agent-specific<sup>10</sup>
- A cohort study by Zheng et al also established the protective effect of early GLP-1RA usage on diabetic retinopathy<sup>8</sup>
- A meta-analysis of data from all cardiovascular outcome studies showed no association between GLP-1 RA treatment and retinopathy per se<sup>11</sup>.
- In general, retinopathy status should be assessed before intensifying any glucose lowering therapy<sup>11</sup>

*To summarise Dear sir/madam to date, the Novo Nordisk assessment of safety data collected from large clinical trial programs, post-marketing surveillance and other relevant sources of information have not shown a causal relationship between semaglutide (or liraglutide) increased risk of retinopathy.*



## Mental Health: Suicidal and self-harm thoughts

- The safety data collected from large clinical trial programs and post marketing surveillance have not demonstrated a causal association between semaglutide or liraglutide and suicidal and self-harming thoughts
- GLP-1RAs are being studied as a potential therapy for mental health disorders like Depression<sup>12</sup> and Alzheimer's Disease\*
- GLP-1RAs are known to show pro-cognitive and neuroprotective properties, and exert modulatory effects on immune, endocrine, and metabolic processes in the central nervous system<sup>12</sup>
- Potential antidepressant effects of GLP-1RAs, especially in the context of their action on the processes related to neuroprotection, inflammation, stress response, energy metabolism, gut-brain crosstalk and the stability of the gut microbiota was discussed in a review article by Dekta j et al<sup>12</sup>
- GLP-1 R Agonists Improves Depression Scores in Diabetes and Obesity - a poster presented in the at OBESITY WEEK<sup>13</sup>
- In addition, Schizophrenia and other psychiatric disorders which are commonly presented with suicidal ideations have also been treated with semaglutide for treating Anti-psychotic induced weight gain and there is also an ongoing clinical trial on the same<sup>14</sup>

*To summarise Dear sir/madam to date, the Novo Nordisk assessment of safety data collected from large clinical trial programs, post-marketing surveillance and other relevant sources of information have not shown a causal relationship between semaglutide (or liraglutide) increased risk mental health.*

## References

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