# GLP-1 Agonists and Ischemic Optic Neuropathy: A Review

Written by The Life Science Feed Editorial Team · Published 13 June 2026 · Edited by Mara Voss

> Glucagon-like peptide-1 (GLP-1) receptor agonists are established therapies for type 2 diabetes mellitus and, increasingly, for weight management. Given their widespread use, clinicians must understand the full spectrum of potential adverse events. Recent post-marketing surveillance and observational studies have raised questions regarding a possible association between GLP-1 receptor agonist use and ischemic optic neuropathy (ION), a condition that can lead to permanent vision loss.

**KEY TAKEAWAYS**

- The Pivot: Observational data indicates a potential association between GLP-1 receptor agonist use and ischemic optic neuropathy.
- The Data: One retrospective cohort study reported an adjusted hazard ratio of 2.13 (95% CI, 1.49-3.04) for ION in GLP-1 receptor agonist users compared to dipeptidyl peptidase-4 (DPP-4) inhibitor users.
- The Action: Clinicians should counsel patients on the symptoms of ION and consider this potential risk, particularly in patients with pre-existing vascular risk factors.

Ischemic optic neuropathy (ION) encompasses conditions resulting from inadequate blood supply to the optic nerve. It is broadly classified into anterior ischemic optic neuropathy (AION) and posterior ischemic optic neuropathy (PION). AION is more common and typically presents with sudden, painless vision loss, often affecting one eye. Risk factors for ION include diabetes mellitus, hypertension, hyperlipidemia, sleep apnea, and structural predispositions such as a 'crowded' optic disc (disc at risk).1

GLP-1 receptor agonists, such as semaglutide, liraglutide, and dulaglutide, exert their glucose-lowering effects by enhancing glucose-dependent insulin secretion, suppressing glucagon secretion, and slowing gastric emptying. They also promote satiety and reduce food intake, contributing to weight loss. These agents are increasingly prescribed due to their efficacy in glycemic control, cardiovascular benefits, and weight reduction.2

## Observational Data on GLP-1 Agonists and ION

The potential link between GLP-1 receptor agonists and ION has emerged from analyses of large healthcare databases and post-marketing surveillance. One retrospective cohort study, published in 2023, investigated the incidence of ION among patients initiating GLP-1 receptor agonists compared to those initiating DPP-4 inhibitors. The study included 1,200,000 patients with type 2 diabetes.3

The primary outcome was a new diagnosis of ION. After adjusting for baseline demographic characteristics and established cardiovascular risk factors, the study reported an adjusted hazard ratio (HR) of 2.13 (95% CI, 1.49-3.04) for

ION in patients using GLP-1 receptor agonists compared to those using DPP-4 inhibitors. The absolute risk difference was 0.07% over a median follow-up of 1.5 years. This translates to approximately 7 additional cases of ION per 10,000 patient-years of GLP-1 receptor agonist exposure.3

Another analysis of the FDA Adverse Event Reporting System (FAERS) database identified a disproportionality signal for ION with GLP-1 receptor agonists. This analysis found a reporting odds ratio (ROR) of 2.5 (95% CI, 2.1-3.0) for ION associated with GLP-1 receptor agonists compared to all other drugs in the database. While FAERS data are subject to reporting bias and do not establish causality, they serve as an important signal for further investigation.4

The proposed pathophysiological mechanisms linking GLP-1 receptor agonists to ION are not fully elucidated. Hypotheses include potential effects on ocular hemodynamics, such as changes in retinal or choroidal blood flow, or alterations in systemic blood pressure that could compromise optic nerve perfusion, particularly in individuals with pre-existing vascular vulnerability. Rapid glycemic control itself has been implicated in transient worsening of retinopathy, but a direct causal link to ION from GLP-1 receptor agonists specifically remains under investigation.5

## Limitations and Clinical Considerations

The available evidence primarily stems from observational studies and pharmacovigilance databases. These study designs are inherently limited by confounding by indication and residual confounding, meaning that patients prescribed GLP-1 receptor agonists may have a higher baseline risk for ION due to unmeasured or inadequately adjusted factors. For example, patients initiating GLP-1 receptor agonists may have more advanced or poorly controlled diabetes, or a higher burden of cardiovascular comorbidities, which are themselves risk factors for ION. Randomized controlled trials, while ideal for establishing causality, are unlikely to be powered to detect rare adverse events such as ION.3,4

Clinicians should be aware of the potential association between GLP-1 receptor agonists and ION. When initiating or continuing GLP-1 receptor agonist therapy, particularly in patients with known risk factors for ION (e.g., diabetes, hypertension, hyperlipidemia, sleep apnea, or a 'disc at risk'), it is prudent to counsel them on the symptoms of ION, which include sudden, painless vision loss in one eye. Patients experiencing such symptoms should be advised to seek immediate ophthalmological evaluation. Further research, including larger prospective observational studies and mechanistic investigations, is warranted to clarify the nature and strength of this association and to identify any specific patient subgroups at higher risk.1,5

For deeper insights into the complex field of endocrinology and diabetes management, including related therapeutic agents, readers might find the Oxford Handbook of Endocrinology and Diabetes invaluable.

> **CLINICAL IMPLICATIONS**
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> The emerging signal linking GLP-1 receptor agonists to ischemic optic neuropathy, while based on observational data, warrants attention from prescribing clinicians. It is a reminder that even highly effective therapies with established cardiovascular benefits can carry less common, but clinically significant, risks. The absolute risk increase appears small, approximately 7 additional cases per 10,000 patient-years, but the consequence of ION (permanent vision loss) is severe. This necessitates a careful, individualized risk-benefit discussion, particularly for patients with multiple pre-existing vascular risk factors or a known 'disc at risk'.
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> For the pharmaceutical industry, this highlights the ongoing importance of robust post-marketing surveillance. As GLP-1 receptor agonists like Novo Nordisk's Ozempic and Wegovy, and Eli Lilly's Mounjaro and Zepbound,

> expand into broader populations, including those without diabetes, the detection of rare adverse events becomes even more critical. The current data, while not definitive for causality, should prompt further investigation and potentially lead to updates in prescribing information to ensure clinicians and patients are fully informed.
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> Patients, especially those with diabetes or obesity, are increasingly aware of GLP-1 receptor agonists. It is incumbent upon healthcare providers to communicate these nuances without causing undue alarm. The benefits of these medicines for glycemic control, cardiovascular risk reduction, and weight management are substantial. However, transparency about potential adverse events, even rare ones, fosters trust and enables shared decision-making. A sudden, painless loss of vision is a medical emergency, and patients on these therapies should be explicitly counselled on this symptom.

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## REFERENCES

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