Clinical Report:

Glucagon-like Peptide-1 Receptor Agonists (GLP-1RAs) and Ocular Health: Guidance for Optometric Practice

American Optometric Association-Evidence-based Optometry Committee

AMERICAN OPTOMETRIC ASSOCIATION

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Overview

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are reshaping the management of chronic diseases, particularly type 2 diabetes mellitus (T2DM), obesity and cardiovascular risk. While originally designed to treat and manage T2DM, these agents provide additional metabolic, cardioprotective, and weight-reduction related benefits. Optimal implementation requires careful patient selection, side effect monitoring, and interdisciplinary collaboration, particularly for patients with ocular, gastrointestinal (GI) or thyroid risk factors.

Given the increasing body of evidence linking GLP-1RAs to potential sight-threatening complications, doctors of optometry must play a pivotal role within the interdisciplinary care team. According to the American Optometric Association (AOA), any patient initiating a GLP-1RA, especially those with diabetes or any form of age-related macular degeneration (AMD), should have an in-person, comprehensive, dilated eye examination either within the 12 months prior to starting therapy or a baseline examination within one month of initiating therapy.

Description of GLP-1 Receptor Agonists

GLP-1RAs are incretin mimetics that activate the GLP-1 receptor (GLP-1R), a G protein-coupled receptor expressed primarily in pancreatic beta cells, as well as in the central nervous system (CNS), GI tract and cardiovascular system. They:

- Stimulate glucose-dependent insulin secretion
- Suppress inappropriate postprandial glucagon release
- Delay gastric emptying
- Promote satiety
- Improve glycemic control and reduce weight

Beyond glycemic modulation, GLP-1RAs have demonstrated significant cardioprotective and nephroprotective effects in individuals with T2DM, independent of their metabolic actions. Clinically, GLP-1RAs are employed in the treatment of T2DM, obesity and, more recently, for potential indications in cardiovascular disease, nonalcoholic steatohepatitis, and neurodegenerative disorders. It is important to note that potent GLP-1RAs, such as tirzepatide and semaglutide, demonstrate greater overall weight loss but are associated with a substantial reduction in lean mass. This should be considered when managing patients, particularly those at risk for sarcopenia or functional decline.

FDA-Approved GLP-1RAs

Generic Name	Brand Name(s)	Approval Year	Dosing	Indications
Exenatide	Byetta, Bydureon BCise	2005/2012/2017	BID/Weekly/Weekly	T2DM adjunct
Liraglutide	Victoza, Saxenda	2010	One time Daily	T2DM, CV risk, Obesity ≥12 y/o
Dulaglutide	Trulicity	2014	One time Weekly	T2DM, CV risk
Lixisenatide	Adlyxin	2016	One time Daily	T2DM adjunct
Semaglutide	Ozempic, Rybelsus, Wegovy	2017–2021	One time Weekly Oral Daily Weekly injection	T2DM, CV risk, Obesity
Tirzepatide	Mounjaro, Zepbound	2022–2023	Weekly injection	T2DM, Obesity, Obstructive Sleep Apnea (OSA)

GLP-1RA Use in the United States

As of 2024, 6% of U.S. adults are actively taking GLP-1RAs, with semaglutide use estimated in 15 million individuals.

- 12% of U.S. adults have used GLP-1RAs at some point
- Among users, 7% use these medications for chronic diseases and 5% for weight loss alone
- In Q4 of 2022, 9 million prescriptions for GLP-1RAs were filled highlighting their growing role (15 million in 2024) in chronic disease and weight management
- There is no published randomized controlled trial or evidence exhibiting higher rates of ophthalmic complications amongst the different GLP-1RAs

Systemic and Ocular Risks of GLP-1RAs

System	Risk	Notes
GI	Nausea, vomiting, diarrhea, constipation	Common; mitigated with slow titration
Pancreatic	Acute pancreatitis	Rare; avoid in patients with a history of pancreatitis
Gallbladder	Cholelithiasis, cholecystitis	Especially with rapid weight loss
Retinal	Worsening diabetic retinopathy	Linked with semaglutide
Optic Nerve	NAION	Very rare but under active investigation
Renal	Acute kidney injury	Usually secondary to dehydration
Thyroid	Medullary thyroid carcinoma (MTC)	Contraindicated in multiple endocrine neoplasia type 2 (MEN-2)/MTC history
Glycemic	Hypoglycemia (with insulin/SUs)	Rare with monotherapy
GI Motility	Gastroparesis exacerbation	Contraindicated in severe cases
Psychiatric	Suicidal ideation	Under review (FDA, EMA, 2025)

Emerging Ocular Risk:

Non-arteritic Anterior Ischemic Optic Neuropathy (NAION)

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common cause of acute optic neuropathy in individuals over 50 years of age. It results from ischemia due to impaired perfusion of the optic nerve head, primarily via the short posterior ciliary arteries. The resultant swelling in the confined space of the optic nerve canal leads to axonal compression and apoptosis of retinal ganglion cells. Optic nerve head drusen can also crowd the disc and should also be considered a risk in patients under 50 years of age.

Risk factors for NAION include:

- Diabetes mellitus
- Hypertension
- Hyperlipidemia
- Obstructive sleep apnea
- Small cup-to-disc ratio aka a "disc at risk" is the strongest risk factor for NAION

Common Signs of NAION

- Sudden, unilateral painless loss of vision
- Visual field defect (usually altitudinal)
- Blurred vision
- Dyschromatopsia (new onset impairment or loss of color vision)
- Relative afferent pupillary defect
- Optic disc swelling with or without hemorrhages

The estimated U.S. incidence ranges from 2.3 to 10.2 per 100,000. NAION is more common in white than Black individuals, likely due to anatomical differences in optic disc morphology.

Evidence Linking GLP-1RAs to NAION

A recent observational study titled "Risk of Non-arteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide" found an association between semaglutide, which is the most prescribed GLP-1RA, and NAION.

On June 6, 2025, the European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) concluded that NAION is a very rare side effect of semaglutide (up to 1 in 10,000 patients). Large epidemiological studies estimate that semaglutide use is associated with a two-fold increased risk of NAION, corresponding to just one additional case per 10,000 person-years.

The EMA has recommended updating semaglutide's product information to include NAION as a very rare side effect. Patients should be advised to report sudden or worsening vision changes, and semaglutide should be discontinued if NAION is confirmed.

EMA recommendations:
- List NAION as a "very rare" side effect
- Seek immediate care for sudden or worsening vision loss
- Discontinue semaglutide (or other GLP-1RAs) if NAION is confirmed

Diabetic Retinopathy (DR) Risks and GLP-1RAs

The **SUSTAIN-6 trial** found an increased rate of DR complications in patients using semaglutide (3.0%) vs placebo (1.8%). Events included:
- Vitreous hemorrhage
- Necessity for retinal laser or intravitreal therapy
- Vision loss

This was likely due to the rapid HbA1c reduction, a known contributor to early worsening of retinopathy. Patients with preexisting DR were especially vulnerable. Rapid glycemic improvement may transiently worsen DR, as noted in the United Kingdom Prospective Diabetes Study (UKPDS).

Emerging Risk: Neovascular AMD

A population-based study of 139,002 patients found:
- Risk of developing neovascular AMD was 0.2% in GLP-1RA users vs 0.1% in non-users
- The relative risk was more than 2x higher for those taking GLP-1RAs
- This accounts for a twofold increased risk of neovascular AMD among GLP-1RA users. Although the absolute risk is low, it warrants surveillance.

Clinical Recommendations for Optometric Care

According to the AOA's Comprehensive Adult Eye and Vision Examination, 2nd Edition, individuals taking GLP-1RAs are considered "at-risk" patients. These patients should:
- Have baseline dilated exams prior to or shortly after initiation of therapy
- Follow more frequent reexamination intervals per Table 2 (copied below), p. 39, Section C
- Receive individualized risk counseling regarding DR, AMD and NAION risk, especially if they have a "disc at risk"
- Collaborative care with providers managing the patient's diabetic and other systemic conditions

Risk Factors for the Development of Eye and Vision Problems

Having a personal or family history of ocular disease.	Having functional vision in only one eye.
Belonging to certain racial and ethnic groups.	Wearing contact lenses.
Having systemic health conditions with potential ocular manifestations (e.g., diabetes mellitus, hypertension, obesity, arteriosclerosis).	Undergoing eye surgery or experiencing previous eye injury.
Participating in occupations that are highly demanding visually or have a high potential of being hazardous to the eyes.	Having high or progressive refractive error.
Taking prescription or nonprescription drugs with ocular side effects.	Experiencing other progressive eye-related health concerns or conditions.

Diabetes Mellitus (DM) in the United States

As of 2023, 15.8% of U.S. adults age 18 and older, or about 38 million U.S. adults, have diabetes, yet nearly 1 in 4 remain undiagnosed. This underscores the importance of optometrists in systemic disease detection. Prevalence increases with age, reaching 27.3% among adults over 60, compared to just 3.6% in those ages 20–39. The data underscore the urgent need for preventative care visits and early detection,

particularly in middle-age and older populations, to avoid complications and improve outcomes through timely intervention and management. These numbers are rising and with it comes an increasing number of NAION cases.

Summary of Medications for DM

Currently, the most prescribed medications for T2D in the United States span several drug classes and reflect both historical patterns and newer therapeutic innovations:

- Metformin, a biguanide, remains the most frequently used first-line therapy, prescribed in tens of millions of cases annually and favored for its efficacy, safety and cardiovascular benefits.
- Sulfonylureas (e.g., glipizide, glimepiride, glyburide) are widely used adjuncts, with millions of prescriptions each year; for instance, glipizide ranked 42nd and glimepiride 64th among all U.S. medications in 2022.
- Insulin (including human and analog formulations like glargine) remains essential, especially in type 1 and advanced type 2 diabetes; it ranks in the top 200 prescribed drugs with over 2 million prescriptions in 2022.
- Dipeptidyl Peptidase IV (DPP 4) inhibitors (e.g., sitagliptin) and Sodium-Glucose Cotransporter-2 (SGLT 2) inhibitors Empagliflozin (Jardiance); Dapagliflozin (Farxiga); Canagliflozin (Invokana); Ertugliflozin (Steglatro); Bexagliflozin (Brenzavvy); and Sotagliflozin (Inpefa) have become prominent, with sitagliptin alone receiving ~7 million prescriptions and ranking among the top 100 U.S. medications.
- GLP-1RAs (e.g., semaglutide, dulaglutide, liraglutide, tirzepatide) are increasingly prescribed due to their glycemic, cardiovascular and weight loss effects; dulaglutide had over 8 million prescriptions in 2022.

Metformin continues as the cornerstone of type 2 diabetes management, but contemporary regimens increasingly incorporate newer agents—GLP-1RAs, SGLT 2 inhibitors, and DPP 4 inhibitors—to optimize glycemic control, reduce cardiovascular/renal risk, and address obesity, each with rising utilization trends among clinicians.

GLP-1RAs Patient Selection:

Ideal Candidates:

- T2DM and obesity
- Those at high cardiovascular risk
- Persons experiencing difficulty with insulin or oral agents
- Nondiabetic patients seeking weight reduction (when approved)

Precautionary Measures:

- Severe GI disease or history of pancreatitis
- Advanced DR
- Patients unable to tolerate injectable medications (oral semaglutide may be considered)

Ophthalmic Risks and Considerations for GLP-1RAs

It is important to have a comprehensive eye examination while taking GLP-1RAs such as semaglutide, liraglutide or tirzepatide due to their potential effects on ocular health, especially in individuals with diabetes or preexisting retinal disease.

Risks and considerations are as follows:

1. Risk of Diabetic Retinopathy Progression

GLP-1RAs are known to improve glycemic control rapidly, and while this is beneficial systemically, the sudden change in blood glucose levels has been associated with a temporary worsening of DR. This phenomenon is not unique to GLP-1RAs but has been observed with intensive insulin therapy as well. In large clinical trials (e.g., the SUSTAIN-6 study), semaglutide was associated with an increased risk of retinopathy complications in patients with preexisting DR. Retinal experts do recommend obtaining a baseline eye exam and considering closer follow up of patients on GLP-1RAs within the first 12 to 18 months of starting the drug, particularly for those who have more severe DR at baseline, high baseline HbA1c percentage, and rapid improvement in glycemic control such as that seen in the SUSTAIN-6 study. This underscores the importance for doctors of optometry on the front line of eye care to protect the vast number of diabetics and non-diabetics who are taking GLP-1RAs.

2. New Onset of Visual Symptoms

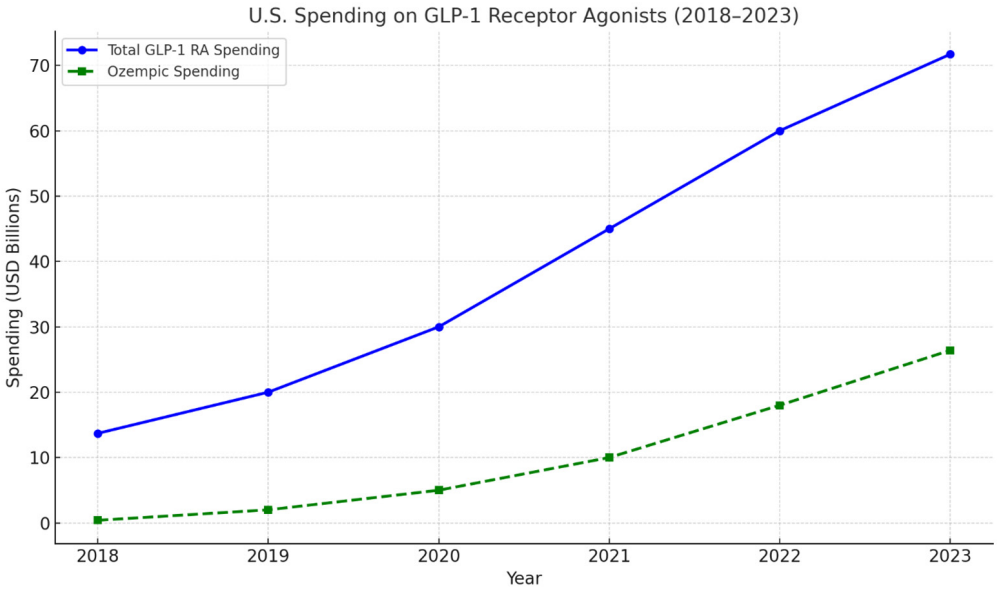
Rapid weight loss or reductions in serum glucose levels from GLP-1RA use can lead to:

- Blurry vision due to changes in refractive error
- Fluctuating vision due to osmotic lens variations
- Metamorphopsia or central scotoma from potential macular edema in diabetic patients

3. New Onset Rare Ocular Adverse Events
Although rare, post-marketing surveillance has reported cases of uveitis, optic neuropathy (in addition to NAION), and diplopia. These are not well-established but highlight the importance of baseline ocular health assessment when initiating any systemic therapy with potential neuro-ophthalmic effects. Doctors should continue to monitor the literature for additional adverse events as more information emerges.

4. Ocular Risk versus Systemic Benefit Tradeoff
While GLP-1RAs exhibit substantial benefits of cardiovascular and renal protection in diabetics, aggressive glycemic management in patients with preexisting ocular disease may place vision at risk. A baseline and follow-up eye exam ensures that ocular risk factors are balanced against systemic gains.

Economic Impact/Spending on GLP-1RAs in the United States
In the United States, spending on GLP-1 receptor agonists has surged dramatically in recent years.



U.S. Spending Trends on GLP-1 Receptor Agonists (GLP-1RAs)
- Pre-2018: Spending on GLP-1RAs was minimal.
- 2018: U.S. spending reached $13.7 billion, marking the start of exponential growth.
- 2018–2023: Total GLP-1RA spending increased five-fold, peaking at $71.7 billion in 2023, a >500% increase.

2023 Spending:
- Semaglutide-based products (Ozempic, Rybelsus, Wegovy) and Tirzepatide (Mounjaro) accounted for approximately 70% of total GLP-1RA expenditures.
- Of this total, 89% was driven by medications approved for type 2 diabetes.
- Ozempic spending alone surged from $0.4 billion in 2018 to $26.4 billion in 2023.
- Overall, U.S. retail prescription drug spending reached approximately $406 billion in 2022 (net of rebates) and grew to $722 billion in 2023—a record 13.6% increase, largely driven by GLP-1RAs.

These figures likely understate the true economic impact, as they exclude certain channels such as compounding pharmacies and manufacturer rebates. Notably, GLP-1RAs are now the fastest-growing category within U.S. prescription drug spending, with projected market expansion continuing through 2027. For perspective, brand-name list prices average approximately $11,000–$12,000 per patient per year.

Eye Care Provider Workforce Projections
From 2020 to 2035, the U.S. ophthalmology workforce is projected to experience a 12% decline in supply (-2,650 full-time equivalent (FTE) ophthalmologists) alongside a 24% increase in demand (+5,150 FTE), resulting in a 30% workforce inadequacy. By 2035, ophthalmology is expected to have the second-lowest workforce adequacy (70%)

among 38 medical and surgical specialties analyzed. Geographic disparities are pronounced, with projected adequacy reaching 77% in metropolitan areas but only 29% in nonmetropolitan regions. Due to the increasing population, increase in disease prevalence and rapidly rising amount of GLP-1RAs prescriptions dispensed, combined with the decreasing population of ophthalmologists relative to the population, there is a greater demand for doctors of optometry to perform in-person, annual, comprehensive, dilated eye examinations on this at-risk population.

Conclusion

GLP-1 receptor agonists are very positive and transformative pharmaceutical agents for chronic disease management; however, they carry potential rare but serious ophthalmic risks, including NAION, DR progression and AMD exacerbation. The rapid rate of change in glycemic control following the initiation of GLP1-RAs has been suggested as a possible factor. Patients over 50 with a "disc at risk" are most at risk for GLP-1RA associated NAION. Annual in-person, comprehensive, dilated eye examinations are more important than ever. Improved patient discussion associated with common systemic disease risk factors such as diabetes, hyperlipidemia, hypertension and others need to occur in greater detail and frequency with patients on or considering GLP-1RAs. Doctors of optometry must remain vigilant, advocate for proactive eye care, and collaborate closely with the broader eye and health care team to prevent vision loss in at-risk patients.

Clinical Recommendations

- Baseline in-person, comprehensive, dilated ocular fundus examination upon starting a GLP-1RA should be performed.
- Baseline ocular fundus photography and possibly OCT for documentation are beneficial for those most at risk.
- Closer follow up and examination of patients on GLP-1RAs within the first 12 to 18 months of starting the medication.
- Advise patients starting a GLP-1RA of the potential ophthalmic complications.
- Advise patients if they have risk factors such as associated systemic diseases, a disc at risk, optic nerve head drusen or worsening DR.
- Advise patients to return to clinic for evaluation immediately for any change in vision.
- If NAION is confirmed, treatment with GLP-1RA should be discontinued, and the patient's health care team should be consulted immediately.

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