

BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

November 2022 • Vol. 19, No. 11

The following succinct analysis appeared in *Pharmacist's Letter*. Based on vol. 38, No. 11

MED SAFETY

You'll hear more buzz about GLP-1 agonists (Victoza, etc) and gallbladder disease...due to recent data and warnings.

Some GLP-1 agonist labels already warn about gallbladder inflammation or stones. Now all of these meds will have this warning.

It's because of a handful of cases reported to FDA over about 15 years...on top of studies suggesting a link. Educate that GLP-1 agonists may increase the risk of gallbladder issues by causing rapid weight loss in some patients.

Put the risk in perspective. About 1 in 370 patients per year on a GLP-1 agonist will have gallbladder or biliary disease...with gallstones in 1 in 715 or gallbladder removal in 1 in 1,100...compared to placebo or other diabetes meds.

Point out that risk seems to go up with longer use of GLP-1 agonists...higher doses...or when they're used for weight loss.

Reassure that GLP-1 agonist benefits generally outweigh risks.

For example, some GLP-1 agonists (*Ozempic, Trulicity, Victoza*) reduce CV risk in patients with type 2 diabetes at high CV risk...and seem to slow progression to albuminuria.

But advise caution with GLP-1 agonists in patients with a history of gallbladder disease...even if they've had their gallbladder removed, since biliary issues (stones, etc) are still possible.

Plus all of these meds also warn of rare pancreatitis.

Counsel that nausea or vomiting is common when starting...but severe, colicky pain can be a red flag for gallbladder issues.

If a patient develops a gallbladder problem on a GLP-1 agonist, advise stopping it...and switching to another diabetes med.

Get our resource, *Drugs for Type 2 Diabetes*, to compare A1c lowering, side effects, and costs of GLP-1 agonists and other meds.

(For more on this topic, see Clinical Resource #381106 at [PharmacistsLetter.com](https://www.pharmacistsletter.com).)

He L, Wang J, Ping F, et al. Association of Glucagon-Like Peptide-1 Receptor Agonist Use With Risk of Gallbladder and Biliary Diseases: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Intern Med.* 2022 May 1;182(5):513-519.

See LEADER NOTES for answers to discussion questions.

DISCUSSION QUESTIONS

OVERVIEW OF CURRENT THERAPY

1. What is known about the risk of gallbladder disease with GLP-1 receptor agonists?
2. What type of study was this?
3. What was the search strategy for identification of information?
4. How were studies selected for inclusion in the meta-analysis?
5. How were data extracted and analyzed from selected studies?

See [LEADER NOTES](#) for answers to discussion questions.

6. How many studies were identified? What was the patient population?

7. What were the results of the meta-analysis?

8. What were the strengths and limitations of the meta-analysis?

9. Were the results expressed in terms we care about and can use?

HOW SHOULD THE NEW FINDINGS CHANGE CURRENT THERAPY?

10. Do the results change your practice? How?

See LEADER NOTES for answers to discussion questions.

APPLY THE NEW FINDINGS TO THE FOLLOWING CASE

DB is a 55-year-old female with a past medical history of type 2 diabetes, coronary artery disease, hypertension, hyperlipidemia, and obesity. For diabetes management, she is currently taking metformin 1,000 mg twice daily. Her A1c today in your office is 8.5% and her BMI is 39 kg/m². She expresses frustration regarding her weight and poorly controlled diabetes.

You discuss options with DB to better control her diabetes. Since she is already on a high dose of metformin, you recommend adding another agent.

11. What are metformin add-on options to improve DB's diabetes management? What are risks and benefits of typical second-line options?

After an in-depth discussion and review of available options, DB chooses to begin Ozempic (semaglutide) in addition to the metformin. She is hoping it will aid in weight loss as well as improvement in her glycemic control.

You counsel DB that nausea and vomiting is common when starting a GLP-1 agonist. But severe, colicky pain can be a red flag for gall bladder issues that can rarely occur with GLP-1 agonists. You also educate DB that these drugs are also associated with rare pancreatitis.

12. What further counsel do you provide to DB regarding weight loss and other options to help her with weight control?

After your discussion, you write DB a weight loss "prescription" to engage in physical activity 4 times a week for 30 minutes and employ a reduced calorie Mediterranean diet of 1,500 kcal/day. She will continue metformin, begin Ozempic, and follow up with you in a month to weigh in and re-evaluate her progress.

See [LEADER NOTES](#) for answers to discussion questions.

REFERENCES

Faillie JL, Yu OH, Yin H, et al. Association of Bile Duct and Gallbladder Diseases With the Use of Incretin-Based Drugs in Patients With Type 2 Diabetes Mellitus. *JAMA Intern Med.* 2016 Oct 1;176(10):1474-1481.

He L, Wang J, Ping F, et al. Association of Glucagon-Like Peptide-1 Receptor Agonist Use With Risk of Gallbladder and Biliary Diseases: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Intern Med.* 2022 May 1;182(5):513-519.

Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011 Oct 18;343:d5928.

Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009 Jul 21;6(7):e1000097.

Woronow D, Chamberlain C, Niak A, et al. Acute Cholecystitis Associated With the Use of Glucagon-Like Peptide-1 Receptor Agonists Reported to the US Food and Drug Administration. *JAMA Intern Med.* 2022 Oct 1;182(10):1104-1106.

Additional Pharmacist's Letter Resources available at [PharmacistsLetter.com](https://www.pharmacistsletter.com)

[Comparison of GLP-1 Agonists.](#) Pharmacist's Letter. August 2019.

[Diabetes Medications: Cardiovascular and Kidney Impact.](#) Pharmacist's Letter. September 2022.

[Improving Diabetes Outcomes.](#) Pharmacist's Letter. March 2019.

[Drugs for Type 2 Diabetes \(United States\).](#) Pharmacist's Letter. July 2022.

[Slowing Progression of Kidney Disease in Patients with Diabetes.](#) Pharmacist's Letter. October 2021.

[Combination Therapy with a GLP-1 Agonist.](#) Pharmacist's Letter. July 2018.

[Weight Loss: Helping Your Overweight and Obese Patients.](#) Pharmacist's Letter. May 2021.

[Weight Loss Products.](#) Pharmacist's Letter. August 2021.

Pharmacist's Letter Journal Club Editors:

Lori Dickerson, PharmD, FCCP, *Editor*; Jennifer Nieman, PharmD, BCPS, *Associate Editor*; Alpa Desai, DO, Department of Community Health & Family Medicine, University of Florida, College of Medicine, Newbury, FL; Lisa D. Mims, MD, Department of Family Medicine, Medical University of South Carolina, Charleston, SC, *Contributing Editors*.

DISCLOSURE:

The editors of this activity and its publisher, Therapeutic Research Center (TRC), have no relevant financial interests related to the products or services covered by this activity. TRC does not receive any commercial support and does not accept any advertising. It is completely independent and is supported entirely by subscriptions. TRC focuses on delivering completely objective, unbiased drug information and advice for the benefit of subscribers.

See LEADER NOTES for answers to discussion questions.