APRIL 2026 | VOLUME 5 | ISSUE 4

Evidence-Based Urgent Care

High-Yield Clinical Education • Practical Application

CLINICAL CHALLENGES:

- What are the currently available weight-loss medications and their mechanisms of action?
- What are the most common side effects from weight-loss medications?
- What are the best treatment options for the common side effects related to weight-loss medications?

Management Considerations for Complications of Weight-Loss Medications in Urgent Care

Authors

Hannah Caplan, DO, MSc
Resident, University of Kansas Medical Center, Kansas City, KS

Tyler Johnson, MD
Medical Education Fellow, Emergency Medicine, University of Kansas Medical Center, Kansas City, KS

Hope Ring, MD, FACEP
Associate Professor, Medical Director of Legacy Urgent Care, University of Kansas Medical Center, Kansas City, KS

Michelle Wilson, MD
Assistant Professor of Emergency Medicine, University of Kansas Medical Center, Kansas City, KS

Peer Reviewers

Erin Loo, PA-C, MHA, FCUCM
Physician Assistant, Integrity Urgent Care, College Station, TX

Ajsa Nikolic, MD, MHA
System Chair of Urgent Care, Occupational Health, and Student Health, Ochsner Health System, New Orleans, LA

Prior to beginning this activity, see "CME Information" on page 2.

Abstract

Given the rising prevalence of obesity and the expanding use of weight-loss treatments, urgent care clinicians must be prepared to recognize and manage potential adverse effects. The most common complaints include nausea, vomiting, diarrhea, and abdominal discomfort, though each medication class carries specific risks and complications. Management strategies vary depending on the medication used and the severity of symptoms. In some cases, discontinuation or dose adjustment may be necessary, while severe complications such as dehydration or pancreatitis may require emergency evaluation. This review provides an overview of the most prescribed weight-loss medications, highlights their potential side effects and complications, and offers evidence-based recommendations for patient management and disposition.

EB MEDICINE

CME Information

Date of Original Release: April 1, 2026. Date of most recent review: March 15, 2026. Termination date: April 1, 2029.

Accreditation: EB Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Credit Designation: EB Medicine designates this enduring material for a maximum of 4 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Specialty CME: Included as part of the 4 credits, this CME activity is eligible for 2 Pharmacology CME credits, subject to your state and institutional requirements.

AAFP Accreditation: The AAFP has reviewed *Evidence-Based Urgent Care* and deemed it acceptable for AAFP credit. Term of approval is from 11/01/2025 to 10/31/2026. Physicians should claim only the credit commensurate with the extent of their participation in the activity. This session, Management Considerations for Complications of Weight-Loss Medications in Urgent Care, is approved for 4.0 enduring material AAFP Prescribed credits.

AOA Accreditation: *Evidence-Based Urgent Care* is eligible for 4 Category 2-B credit hours per issue by the American Osteopathic Association.

Needs Assessment: The need for this educational activity was determined by a practice gap analysis; a survey of medical staff; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation responses from prior educational activities for urgent care and emergency medicine physicians.

Target Audience: This internet enduring material is designed for physicians, physician assistants, nurse practitioners, and residents in the urgent care and family practice settings.

Goals: Upon completion of this activity, you should be able to: (1) identify areas in practice that require modification to be consistent with current evidence in order to improve competence and performance; (2) develop strategies to accurately diagnose and treat both common and critical urgent care presentations; and (3) demonstrate informed medical decision-making based on the strongest clinical evidence.

CME Objectives: Upon completion of this activity, learners should be able to: (1) classify the currently available weight-loss medications by their mechanisms of action and indications for usage; (2) evaluate whether a patient presentation in the urgent care setting may be related to the weight-loss medication they are on and consider what diagnosis may be more likely ; and (3) determine treatment options for the common side effects and adverse outcomes potentially related to weight-loss medications.

Discussion of Investigational Information: As part of the activity, faculty may be presenting investigational information about pharmaceutical products that is outside of Food and Drug Administration approved labeling. Information presented as part of this activity is intended solely as continuing medical education and is not intended to promote off-label use of any pharmaceutical product.

Disclosure: It is the policy of EB Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME activities. All individuals in a position to control content have disclosed all financial relationships with ACCME-defined ineligible companies. EB Medicine has assessed all relationships with ineligible companies disclosed, identified those financial relationships deemed relevant, and appropriately mitigated all relevant financial relationships based on each individual's role(s). Please find disclosure information for this activity below:

Planners

- Tracey Quail Davidoff, MD (Editor-in-Chief):
  - AstraZeneca (consultant/advisor)
  - GSK (consultant/advisor)

Faculty

The faculty for this activity have no relevant financial relationships with ineligible companies.

- Hannah Caplan, DO (Author)
- Tyler Johnson, MD (Author)
- Hope Ring, MD (Author)
- Michelle Wilson, MD (Author)
- Erin Loo, PA-C (Peer Reviewer)
- Ajsa Nikolic, MD (Peer Reviewer)
- Bradley Laymon, PA-C (Coding Challenge Author)
- Anneke Smith, MS (Content Editor)
- Dorothy Whisenhunt, MS (Content Editor)

Earning Credit: Learners can earn credit by going to www.ebmedicine.net and selecting the test they wish to complete. To receive credit, they must score 100% on the test and complete the evaluation. After completing these steps, a CME certificate will be emailed to them.

Additional Policies: For additional policies, including our statement of conflict of interest, source of funding, statement of informed consent, and statement of human and animal rights, visit https://www.ebmedicine.net/policies

EVIDENCE-BASED AI-FREE CONTENT PEER-REVIEWED

At EB Medicine, we produce content for emergency medicine and urgent care clinicians that is evidence-based and peer reviewed, and at the same time infused with an understanding of the realities of clinical practice, human behavior, and institutional and social limitations that only humans can apply. For these reasons, EB Medicine assures our readers and subscribers that all authors of our content have certified that they have not used generative AI-assisted technology in the writing of their manuscript and that clinical pathways and images are human-designed. For more information, visit www.ebmedicine.net/AI-statement

QUICK READ

Points & Pearls

APRIL 2026 | VOLUME 5 | ISSUE 4

Management Considerations for Complications of Weight-Loss Medications in Urgent Care

Points

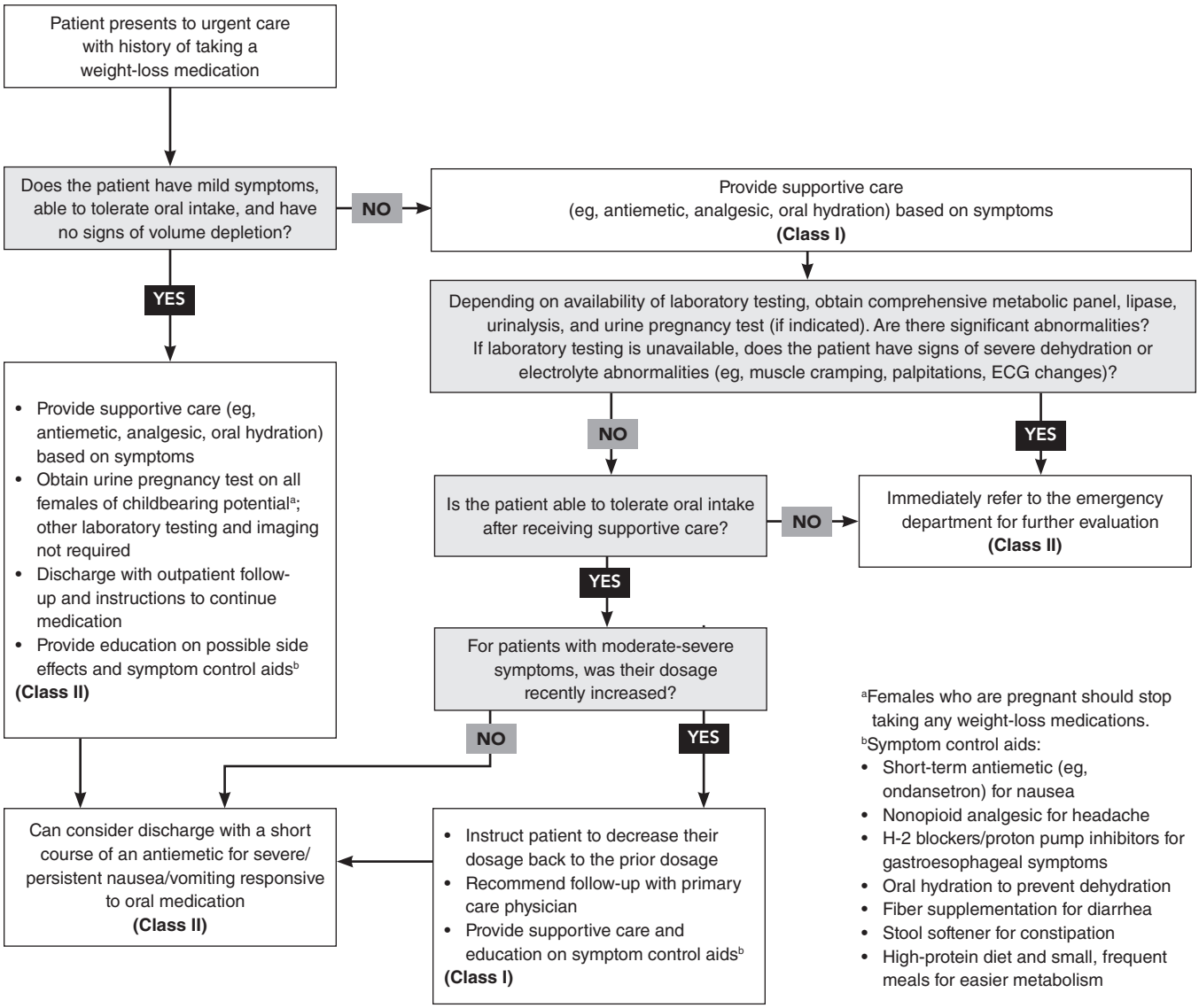
- The most common prescription weight-loss medications include glucagon-like peptide-1 (GLP-1) receptor agonists, dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists, sympathomimetic amines such as phentermine, combination therapies of sympathomimetic amines, and lipase inhibitors.
- The most common side effects of weight-loss medications, particularly GLP-1 receptor agonists, are gastrointestinal symptoms, including nausea, vomiting, diarrhea, and constipation.[7] **(See Table 2.)**
- Consider medication adverse effects in patients presenting with unexplained gastrointestinal symptoms, especially if they are using a weight-loss medication.
- Clinicians should review the medication name, dose, route of administration, start date, and recent dose changes to determine if symptoms correlate with therapy.
- Red-flag symptoms include persistent vomiting, severe abdominal pain, or inability to tolerate oral intake. These presentations warrant evaluation at a higher level.
- Diagnostic testing may not be necessary for patients with mild symptoms who are able to tolerate oral intake and who improve with supportive care.[7]
- For patients with moderate or severe symptoms, laboratory testing, including a comprehensive metabolic panel and lipase to assess for electrolyte abnormalities, renal dysfunction, and pancreatitis, may be considered. A urinalysis may help assess hydration status and ketonuria, and a urine pregnancy test in patients who have a uterus can rule out early pregnancy symptoms.
- Rare but serious complications such as pancreatitis, gallbladder disease, hyperkalemia, and diabetic ketoacidosis can occur in patients taking weight-loss medications.[9-12,14]
- Phentermine-containing medications can cause hypertension and tachycardia, and should be considered when evaluating patients with palpitations, headache, or elevated blood pressure.
- Naltrexone-bupropion lowers the seizure threshold, making it potentially unsafe for patients with seizure disorders, eating disorders, or abrupt alcohol or benzodiazepine withdrawal.[6]
- Orlistat commonly causes gastrointestinal effects such as steatorrhea and fecal urgency, particularly when dietary fat intake is high.[6]

Pearls

- Dose escalation is a common trigger for side effects, as symptoms are most likely to occur during the first month of therapy or after a dose increase. Dose reduction to a previously tolerated level may improve symptoms.
- You may need to ask about weight-loss medications specifically, as patients may not volunteer information about taking a weight-loss medication, particularly if it was obtained online, via a compounding pharmacy, or outside the healthcare system.
- Short-term antiemetic therapy (eg, ondansetron) can be used for persistent nausea or vomiting.
- If a patient is able to tolerate liquids, an oral hydration solution may be administered in the clinic. Intravenous fluids may be necessary when a patient cannot tolerate oral intake.
- Injection-site reactions and dermatologic complications can occur with GLP-1 receptor agonists, ranging from mild pruritus to severe allergic reactions.
- Some patients may have been prescribed a weight-loss medication online without appropriate counseling on the expected side effects. Consider creating patient education handouts that your clinic can distribute that explains typical and atypical adverse effects of weight-loss medication use.

Clinical Pathway for Urgent Care Management of Complications in Patients Taking Weight-Loss Medications

Click or scan for interactive pathway



[a]Females who are pregnant should stop taking any weight-loss medications.

[b]Symptom control aids:
- Short-term antiemetic (eg, ondansetron) for nausea
- Nonopioid analgesic for headache
- H-2 blockers/proton pump inhibitors for gastroesophageal symptoms
- Oral hydration to prevent dehydration
- Fiber supplementation for diarrhea
- Stool softener for constipation
- High-protein diet and small, frequent meals for easier metabolism

Class of Evidence Definitions

Each action in the clinical pathways section of *Evidence-Based Urgent Care* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Case Presentations

CASE 1

A 45-year-old man presents to urgent care with fatigue, muscle cramps, and light-headedness for the past 2 days...

- The patient has a history of hypertension and obesity.
- His vital signs include: temperature 98.2˚F; heart rate, 92 beats/minute; blood pressure, 108/66 mm Hg; respiratory rate, 16 breaths/minute; oxygen saturation, 99% on room air.
- He denies chest pain, palpitations, shortness of breath, nausea and vomiting, or diarrhea.
- He notes that he is on lisinopril and started semaglutide 3 months ago for weight loss.
- Based on his medication list, you consider what diagnoses are more likely…

CASE 2

A 38-year-old man presents to urgent care for nausea and vomiting and epigastric discomfort...

- He has a history of type 2 diabetes mellitus and is currently on semaglutide.
- His vital signs are: temperature, 98.9˚F; heart rate, 105 beats/minute; blood pressure, 118/72 mm Hg; respiratory rate, 16 breaths/minute; oxygen saturation, 96% on room air.
- On examination, he has tenderness to palpation of the epigastric area, without rebound tenderness or guarding.
- While attempting to get his symptoms under control with fluids and antiemetics, you consider what workup should be obtained…

CASE 3

A 29-year-old woman presents to urgent care with headache, flushing, and palpitations...

- She has a history of obesity and anxiety but no history of hypertension. She denies chest pain, shortness of breath, blurry vision, or neurologic deficits.
- She reports starting phentermine 2 weeks ago for weight loss.
- Vital signs reveal: temperature, 97.9˚F; heart rate, 112 beats/minute; blood pressure, 172/98 mm Hg; respiratory rate, 18 breaths/minute; oxygen saturation, 98% on room air.
- On examination, her heart and lungs are normal, and she has no focal neurologic deficits.
- While attempting to get her symptoms under control with fluids and analgesics, you consider what the cause of her newly elevated blood pressure is...

■ Introduction

Obesity, defined as a body mass index (BMI) of >30 kg/m², is a significant public health concern, affecting a large proportion of the population in the United States and worldwide. It is associated with an increased risk for developing chronic diseases such as type 2 diabetes mellitus, obesity-related cancers, chronic back issues, exacerbation of chronic lower extremity arthritis, hypertension, and hyperlipidemia. Multiple pharmacologic therapies have recently emerged as options for weight management.[1] Commonly used weight-loss medications include glucagon-like peptide-1 (GLP-1) receptor agonists, dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor agonists, lipase inhibitors, sympathomimetic-antiepileptic combinations, and opioid antagonist-antidepressant combinations.

While these medications offer a nonsurgical approach to weight management, they are also associated with various potential adverse effects that may prompt urgent care (UC) visits. Complications and side effects of weight-loss medications range from mild gastrointestinal symptoms to more severe issues, including dehydration, pancreatitis, or metabolic/electrolyte imbalances.[2] Given the increasing popularity of these medications, UC clinicians must be equipped to recognize and manage potential complications. This issue of *Evidence-Based Urgent Care* reviews common UC presentations related to weight-loss medications, with recommendations on appropriate evaluation and management.

■ Etiology and Pathophysiology

Obesity rates have been rising at an alarming rate, posing a significant public health challenge. In 2022, there were an estimated 107 million adults living with obesity in the United States, representing a staggering 42.5% of the adult population. This is an increase from 34.7 million adults in 1990 (19.3% of the adult population). By 2035, the percentage of adults with obesity is projected to increase to 126 million, or 46.9%.[3] This growing prevalence is linked to an increased burden of obesity-related comorbidities, including type 2 diabetes mellitus, hypertension, and

cardiovascular disease.[4]

In response to the obesity epidemic, pharmacologic interventions have become an increasingly utilized alternative to bariatric surgery.[5] Among 11.2 million adults with obesity, antiobesity medications were prescribed to 2.9% of patients in 2019 compared with 1.1% in 2010.[5] Several different classes of weight-loss medications are currently in use, each targeting different physiological pathways involved in appetite regulation, metabolism, and fat absorption. The most widely prescribed first-line agents and their medication classes are listed in **Table 1**.

GLP-1 receptor agonists work by mimicking the incretin hormone, glucagon-like peptide-1, which

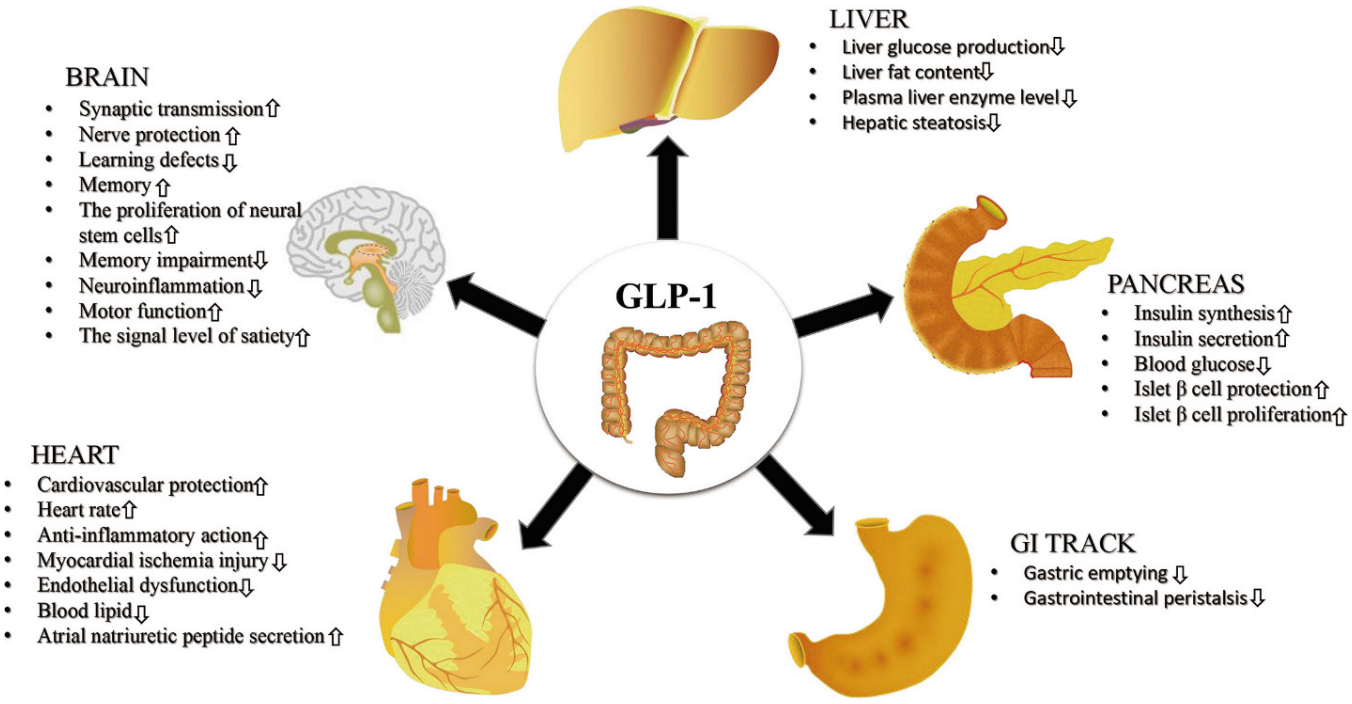
Table 1. Common Prescription Weight-Loss Medications and Their Physiological Pathways[1,6]

Medication Class	Generic Names	Physiological Pathway
GLP-1 receptor agonists	• Semaglutide • Liraglutide	• Mimics GLP-1 • Suppresses glucagon release • Slows gastric emptying • Increases glucose-dependent insulin secretion
Dual GIP agonist/GLP-1 receptor agonist	• Tirzepatide	• Suppresses glucagon release • Slows gastric emptying • Addition of GIP agonist is believed to increase insulin secretion and lead to even further reduced appetite and improve fat metabolism
Lipase inhibitors	• Orlistat	• Blocks enzymes (lipases) in the gut from breaking down dietary fats, preventing absorption and promoting satiety
Sympathomimetic amines	• Phentermine	• Mimics the effects of the sympathetic nervous system • Boosts natural neurotransmitters such as adrenaline (stimulant) • For short-term weight loss
Combination therapies	• Phentermine-topiramate • Naltrexone-bupropion	• Acts as an appetite suppressant • Increases the release of norepinephrine in the brain

www.ebmedicine.net

Abbreviations: GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1.

Figure 1. Glucagon-Like Peptide-1 Receptor Agonist Mechanisms of Action



enhances glucose-dependent insulin secretion while suppressing glucagon release, slowing gastric emptying, and increasing satiety through central appetite regulation.[7] **See Figure 1 on page 6** for the mechanism of action of GLP-1 receptor agonists. This class of medications has demonstrated significant efficacy in weight-loss, with trials showing reductions of up to 15% of baseline body weight.[8] Tirzepatide is a novel dual GIP and GLP-1 receptor agonist. Tirzepatide enhances insulin secretion, suppresses glucagon release, and delays gastric emptying.

Orlistat, a lipase inhibitor, prevents dietary fat absorption by inhibiting pancreatic lipases, leading to calorie deficit-induced weight-loss.[6] Phentermine, a centrally acting stimulant, promotes weight-loss by increasing norepinephrine release, leading to appetite suppression.[6] Phentermine is often combined with topiramate, an antiepileptic medication that has been found to further enhance weight reduction through mechanisms that include modulation of gamma-aminobutyric acid (GABA) activity.[1] Naltrexone-bupropion exerts its effects via the hypothalamic melanocortin system and mesolimbic reward pathways, decreasing food intake while reducing cravings.[2]

As the prevalence of obesity and the use of pharmacologic treatments continue to increase, UC clinicians will encounter more patients experiencing complications from these medications. A thorough understanding of their mechanisms and potential adverse effects is critical for effective patient management in the UC setting. Approved weight-loss medications are summarized in **Table 2**.

■ Differential Diagnosis

When evaluating patients in the UC setting who present with symptoms potentially related to weight-loss medications, it is critical to consider both the most common and the most serious adverse effects

Table 2. United States Food and Drug Administration-Approved Medications for Weight Loss

Generic Name	Mechanism of Action	Approved for	Year Approved for Obesity Treatment	Route and Frequency of Administration	Contraindications of Use	Most Common Side Effects
Orlistat	Prevents dietary fat absorption	Adults and children aged ≥12 years	1999 for adults; 2003 for children aged ≥12 years	Oral, 3 times daily with meals containing fat	Malabsorption syndromes or cholestasis	• Increased flatus • Oily/loose stools
Phentermine-topiramate	Leads to appetite suppression	Adults and children aged ≥12 years	2012 for adults; 2022 for children aged ≥12 years	Oral, once daily	Glaucoma, hyperthyroidism, or taking MAOI	• Dry mouth • Constipation • Paresthesia • Taste alterations • Insomnia • Elevation in heart rate
Naltrexone-bupropion	Reduces food cravings	Adults	2014	Oral, twice daily (after dose escalation)	Uncontrolled hypertension, seizures, eating disorders, taking MAOI, or alcohol/opioid use	• Nausea • Constipation • Headache • Dizziness • Dry mouth
Liraglutide	Slows gastric emptying to lead to decreased appetite	Adults and children aged ≥12 years	2014 for adults; 2020 for children aged ≥12 years	Subcutaneous injection, once daily	Personal or family history of thyroid cancer (MTC or MEN2)	• Nausea • Diarrhea • Vomiting
Semaglutide	Slows gastric emptying, which leads to decreased appetite	Adults and children aged ≥12 years	2021 for adults; 2022 for children aged ≥12 years	Subcutaneous injection, once weekly; oral, once daily	Personal or family history of thyroid cancer (MTC or MEN2)	• Nausea • Vomiting • Diarrhea • Constipation • Headache
Tirzepatide	Slows gastric emptying, which leads to decreased appetite	Adults	2023	Subcutaneous injection, once weekly	Personal or family history of thyroid cancer (MTC or MEN2)	• Nausea • Vomiting • Diarrhea

www.ebmedicine.net

Abbreviations: MAOI, monoamine oxidase inhibitor; MEN2, multiple endocrine neoplasia type 2; MTC, medullary thyroid cancer.

associated with these treatments.

The most frequently reported adverse effects of GLP-1 receptor agonists (eg, semaglutide, liraglutide, and tirzepatide) are gastrointestinal in nature, including nausea, vomiting, diarrhea, and constipation.[7] While these symptoms are generally mild and self-limited, more severe complications have been reported. Pancreatitis is a known but rare adverse effect associated with GLP-1 receptor agonists, with multiple case reports describing patients developing acute pancreatitis following initiation of the medication.[9,10] Additionally, there is emerging evidence suggesting a potential link between hyperkalemia and GLP-1 receptor agonist use. A population-based cohort study found an incidence rate of 22.1 events per 1000 person-years, with an absolute cumulative 3-year risk for hyperkalemia at 5.7% among users.[11] Appendicitis has also been reported in association with semaglutide use, with the United States Food and Drug Administration (FDA) Adverse Event Reporting System identifying 10 serious cases (0.56%) and 2 nonserious cases (0.05%) between 2018 and 2022.[12] Though causality has not been definitively established, it has been hypothesized that GLP-1 receptor agonist-induced gastrointestinal effects, including delayed gastric emptying and increased risk for fecalith formation, may contribute to appendicitis.[12] While both tirzepatide and semaglutide are used for weight loss and have a similar side effect profile overall, tirzepatide also activates GIP receptors, which may contribute to additional metabolic effects.[13] In addition to gastrointestinal side effects, GLP-1 receptor agonists have been associated with increased risk for cholelithiasis and cholecystitis.[14]

Semaglutide has the greatest side effect profile.[7] Semaglutide symptomology is most commonly nausea, diarrhea, vomiting, and constipation, when compared with liraglutide and dulaglutide. Liraglutide more commonly causes upper abdominal pain and carries a higher risk for pancreatitis.[7] While GLP-1 receptor agonists are associated with a variety of side effects **(see Table 2, page 7)**, they do not typically cause severe abdominal pain.[6] New-onset severe abdominal pain warrants further evaluation, as does an abrupt increase in vomiting.[15]

Other weight-loss medications, besides GLP-1 receptor agonists, carry distinct risks. Orlistat, a lipase inhibitor that prevents fat absorption, is primarily associated with gastrointestinal side effects, including steatorrhea, fecal urgency, and increased flatulence due to undigested fat passing through the gastrointestinal tract.[6] While less common, there have been reports of hepatic injury linked to orlistat use, prompting the FDA to issue warnings regarding rare cases of severe liver injury.[1] Phentermine-topiramate, a sympathomimetic and antiepileptic combination, is associated with neurological symptoms such as paresthesia, dizziness, and dysgeusia, as well as increased heart rate and blood pressure.[6] Topiramate also presents a well-documented risk for teratogenicity, necessitating effective contraception in women of childbearing potential.[1] Naltrexone-bupropion, a combination therapy affecting central appetite regulation, commonly leads to nausea, vomiting, headache, and insomnia.[2] More serious concerns include hypertension and seizures, as bupropion lowers the seizure threshold, particularly for patients with a history of seizures or eating disorders.[6]

■ Urgent Care Evaluation

History

When assessing patients presenting with potential side effects from a weight-loss medication, critical questions to ask include:

- The prescribed medication and associated dosage;
- Date the medication was initiated;
- Date of the patient's last dose of the medication; and
- Any changes to the dosage.

The patient's medication history should be reviewed and include over-the-counter medications and supplements. Some patients may be reluctant to disclose medications they have purchased outside of the mainstream health system, such as online brokers, compounding pharmacies, or even internationally. A full review of symptoms and their onset and duration is an additional, critical portion of the history, given various weight-loss medications have varying side-effect profiles. For all side effects related to weight-loss medications, particularly GLP-1 receptor agonists, symptoms are most prominent during the first month of therapy and/or with dosage increases but tend to dissipate over time.[7]

Obtaining a thorough, accurate history is important, as severe complications can arise if conditions associated with GLP-1 receptor agonist use develop (eg, pancreatitis, gallbladder/biliary disease, bowel obstructions) and are not diagnosed and treated appropriately.[7] Be sure to ask the patient questions about their pain, including character, location, frequency, relation to food intake, and associated symptoms. Patients with a history of gastroesophageal reflux disease (GERD) may experience transiently worsening symptoms, and patients without a history of GERD may develop symptoms associated with GLP-1 receptor agonist use.[15] Questions regarding heartburn, regurgitation, burning sensation in the throat, sour taste in the mouth, and timing of symptoms in relation to food intake and position, are important.

In the setting of persistent vomiting or diarrhea, assessing the amount of volume loss along with the amount of oral intake can factor into the level of

dehydration suspected. Severe dehydration through volume loss or decreased oral intake can induce a prerenal acute kidney injury, especially for patients with hypertension or those prescribed nephrotoxic drugs. Ask about dizziness on standing, amount of urine output (including last void), dry mouth, and any previous renal history.

Injectable weight-loss medications, specifically the GLP-1 receptor agonists, have been associated with a spectrum of dermatologic complications ranging from mild injection-site symptoms (eg, pruritus, warmth at the injection site) to rare immune-mediated reactions such as urticaria and edema after injection.[7] T-cell mediated dermatologic reactions have occurred as well, resulting in formation of pustular, vesicular, or psoriasiform eruptions.[7] Clinicians should specifically ask about timing of symptom onset relative to injections, injection-site location and technique, and any prior history of drug reactions or autoimmune skin disease.

Physical Examination

The physical examination, while focused, should include vital signs (ie, temperature, heart rate, blood pressure, respiratory rate, oxygen saturation); volume status via assessment of mucous membranes; skin turgor; and capillary refill; and a thorough abdominal examination. The abdominal examination should include inspection, auscultation, and palpation to assess for tenderness, rebound, guarding, or rigidity. Observe whether the patient is able to stand up straight and ambulate, or if they require assistance due to discomfort. Given the risk for dermatologic complications, any skin complaints should be carefully examined and documented.

■ Diagnostic Studies

In the UC setting, patients may not require diagnostic laboratory testing or imaging if symptom severity is mild, the patient feels improved with oral medication, is tolerating oral intake, and there are no signs of volume depletion or acute abdominal findings. For those with more severe symptoms or signs of volume depletion, testing is warranted. Testing should include a complete metabolic panel to evaluate liver and kidney function and electrolyte abnormalities. Lipase should be included if pancreatitis is suspected. A urinalysis may help assess hydration status and identify ketonuria, which may signal inadequate caloric intake or early metabolic disturbances. Additionally, a urine pregnancy test is important because early pregnancy symptoms such as nausea, vomiting, and fatigue can resemble or obscure medication-related effects. These results will help determine the patient's stability and assess whether the severity of their condition warrants further evaluation in the emergency department (ED).

If symptoms are severe, the patient may require imaging, more aggressive symptom management, and possible hospital admission.[7] The need for diagnostic imaging with ultrasound to assess for gallbladder/biliary disease or computed tomography scans to assess for pancreatitis or bowel obstructions may warrant ED evaluation, unless imaging capabilities are readily available.

■ Treatment

Treatment options for the side effects of weight-loss medications should focus on symptom control and dietary modifications. For patients who recently had their GLP-1 receptor agonist dosage increased and side effects are significant, they can decrease the dose to their prior dosage and follow up with their prescribing physician.[15] For severe side effects, cessation of the medication is advised until proper follow-up is possible.[15]

Medications

Medications may include antiemetics, analgesics, and H-2 blockers or proton pump inhibitors. Antiemetics should be used only in the short-term, if the patient presents with persistent or severe gastrointestinal side effects.[15] The most common antiemetic used is ondansetron. Metoclopramide, while not absolutely contraindicated, should not be a first-line option, given its mechanism of action. It can accelerate gastric emptying, which can be counterproductive to the mechanism of weight-loss medications. Options for analgesia vary among clinicians, but opioids should be avoided, given the risk for dependence and worsening nausea and constipation. For patients with transient worsening of their GERD or with new onset of GERD, an H-2 blocker or proton pump inhibitor may be used short-term.[15]

Dietary Modifications

Dietary modifications can play a role in preventing worsening dehydration and help improve symptomology. Counseling patients on increasing fiber intake and adding stool softeners can assist with constipation.[15] Fiber intake can be increased with fiber-rich foods or fiber supplementation. High-protein diets, specifically low-fat proteins, are an additional dietary modification for patients taking GLP-1 receptor agonists because protein delays gastric emptying and low-fat proteins are broken down more easily, preventing symptoms associated with GLP-1 receptor agonists.[16] High-protein diets also help prevent loss of lean muscle mass and can help maintain long-term weight loss for patients taking GLP-1 receptor agonists.[17]

Oral hydration may play a key role in prevention of acute kidney injury and other electrolyte derangements, as these most commonly arise due

to volume depletion.[7] For patients showing signs of severe dehydration, acute kidney injury, or who are unable to tolerate oral intake, intravenous fluids should be administered. If your facility is not capable of intravenous fluid rehydration, the patient may require treatment in the ED. Other dietary modifications such as decreasing the volume of food intake and mindfulness of satiety can help improve nausea/vomiting and constipation associated with weight-loss medications.[15,16,19]

■ Special Populations

Pediatric Patients

Obesity is one of the most common pediatric chronic illnesses, affecting 14.4 million children and adolescents.[4] Childhood obesity is correlated with obesity in adulthood, cardiovascular disease, prediabetes, and poor psychological and emotional health. Orlistat, phentermine-topiramate, semaglutide, and liraglutide have been FDA approved as weight-loss medications for children aged ≥12 years.[8] Pharmacologic treatment should be in combination with lifestyle changes and counseling. It is important to note that if a child's nutrition is not closely supervised, reduced appetite can lead to inadequate caloric intake, growth deceleration, and delayed puberty.[18]

Older Patients

Older patients aged ≥65 years require special consideration when taking weight-loss medications, due to higher risk for dehydration, acute kidney injury, and worsening gastroparesis, especially when combined with polypharmacy and reduced physiologic reserve. In addition, older patients are more vulnerable to lean muscle loss, frailty, and falls.[19] For these patients, UC clinicians should maintain a lower threshold for ordering laboratory testing, administering hydration, adjusting medication dosages, and referring patients to the ED.

Patients With Diabetes

Patients with diabetes taking weight-loss medications need close monitoring because rapid glucose improvement can cause hypoglycemia, especially when combined with insulin or sulfonylureas. In UC, checking glucose, assessing hydration, reviewing a patient's full diabetes medication regimen, and watching for ketosis, including diabetic ketoacidosis (DKA), are essential. An additional area of concern to be aware of in diabetic patients are complications related to diabetic retinopathy. Citing low-quality evidence, prescribing information for GLP-1 receptor agonists suggests a higher incidence of worsening diabetic retinopathy and vitreous hemorrhages for patients who already have diabetic retinopathy.[20] A case report recommends that diabetic retinopathy should not preclude the use of GLP-1 receptor agonists.[21] The UC clinician should be mindful of diabetic patients on GLP-1 receptor agonist medications presenting with eye complaints potentially needing urgent ophthalmologic evaluation.

Patients Undergoing Anesthesia

Safety concerns exist regarding the use of GLP-1 receptor agonists in the perioperative period due to the delayed gastric emptying and potential for residual gastric contents beyond traditional fasting intervals before surgery. Additionally, while GLP-1 receptor agonist medications alone seldom cause hypoglycemia, the risk arises when they are used in the setting of extended fasting. Current multisociety guidelines from the American Society of Anesthesiologists, American Society for Metabolic and Bariatric Surgery, and the American Gastroenterological Association recommend holding GLP-1 receptor agonists in the perioperative period based on shared decision-making that accounts for individual patient risk.[22] This risk assessment should include whether the patient is in the escalation phase of GLP-1 receptor agonist use, how high their dose is, the presence of symptoms suggestive of delayed gastric emptying, and concurrent conditions leading to delayed gastric emptying.[22] For UC clinicians performing preoperative clearances, they should instruct the patient to discuss how long their GLP-1 receptor agonist should be held with the anesthesiologist and/or surgeons involved in the operative period, as this is a risk-benefit discussion based on the patient's individual risk factors. Potential approaches include holding the medication for 1 week prior to surgery or to follow a liquid diet 24 hours prior to surgery to mitigate aspiration risks.[22]

■ Controversies and Cutting Edge

The rapid rise in popularity and clinical use of GLP-1 receptor agonists and other medications for weight loss have introduced a range of complex and evolving controversies that clinicians and patients must navigate. These challenges span from medication sourcing and safety concerns, issues of access, off-label use, and long-term outcomes.

Shortages

The surge in demand for GLP-1 receptor agonist medications has led to widespread shortages of FDA-approved versions of the medications. While compounded versions have been allowed on the market, given the shortage of these drugs, patients should be aware that compounded versions do not undergo FDA review for safety or effectiveness prior to being marketed. There have been some reports related to adverse events secondary to dosing errors from incorrect patient self-administration and healthcare professionals miscalculating doses of these compounded products.[23]

Off-Label Use

The cultural spotlight on GLP-1 receptor agonists has driven widespread off-label use, and a black market has emerged where products may be misbranded, contain inaccurate dosages, or be adulterated with undeclared substances.[19] These medications are also available over-the-counter from other countries, including compounded forms. Patients may not disclose their use of nonprescribed medications, complicating clinical care. Further, patients may not have been counseled on side effects, proper diet, or offered preventative nausea medications, making them more likely to present to UC without knowledge of GLP-1 receptor agonist complications. Data on the prevalence of GLP-1 receptor agonist misuse are currently lacking.

Cost

The high cost of these medications raises concerns for equitable access. Insurance companies typically require preauthorization, and out-of-pocket costs remain high.

Long-Term Use

Given that the use of GLP-1 receptor agonist medications for weight loss is recent, there are a relative lack of data regarding long-term use effects. Multiple studies report that stopping GLP-1 receptor agonists leads to weight regain, often proportional to how much was lost on the drug. In a 2025 meta-analysis of 8 randomized controlled trials, the average weight regained after stopping was 2.2 kg for liraglutide and 9.7 kg for semaglutide/tirzepatide.[24] Another analysis of 44 studies estimated people regain about 76% of the weight they lost, plateauing below their original weight, suggesting some long-term benefit.[25]

Microdosing

Microdosing of GLP-1 receptor agonists is a growing but off-label practice involving patients taking smaller-than-standard doses. Patients commonly microdose to minimize gastrointestinal side effects, reduce cost by stretching expensive medications, manage supply shortages, or maintain weight

5 Things That Will Change Your Practice

1. **Recognize the risk for hyperkalemia in patients using GLP-1 receptor agonists concurrently with ACE inhibitors.** Hyperkalemia has been observed in patients using GLP-1 receptor agonists.[11] The risk for hyperkalemia is increased for patients with coexisting renal impairment or concurrent medications that raise potassium levels (such as ACE inhibitors). Draw labs and monitor potassium levels for patients presenting with weakness or cardiac symptoms.

2. **Screen for undisclosed or nonprescribed weight-loss medication use, including compounded or black-market GLP-1 receptor agonist agents.** Patients may not disclose the use of weight-loss medications, particularly non–FDA-approved GLP-1 receptor agonists. These products may have uncertain dosing or formulation that could lead to adverse events such as gastrointestinal symptoms, dehydration, electrolyte abnormalities, and delayed gastric emptying. UC clinicians should specifically ask about injectable or oral weight-loss medication use when evaluating patients with unexplained nausea, vomiting, abdominal pain, or metabolic derangements.

3. **Consider cardiovascular complications and risks in patients taking phentermine-topiramate.** Phentermine-topiramate is associated with increased heart rate and blood pressure, which may pose a risk to patients with comorbidities such as hypertension, arrhythmias, or coronary artery disease.[6] UC clinicians should assess vital signs and cardiovascular history before recommending continued use in symptomatic patients. UC clinicians should also take into consideration the use of phentermine-containing weight-loss medications as a potential exacerbating factor of cardiovascular symptoms.

4. **Recognize the risk for seizure with naltrexone-bupropion use in at-risk populations.** Bupropion lowers the seizure threshold, making the naltrexone-bupropion combination potentially dangerous for patients with a history of seizures, eating disorders, or abrupt alcohol/benzodiazepine withdrawal.[2]

5. **Assess for dehydration in patients taking weight-loss medications.** Although nausea, vomiting, and diarrhea are common complaints in patients using weight-loss medications, patients presenting with tachycardia or dry mucous membranes may be dehydrated. A trial of oral fluid rehydration is indicated, and care may need to be escalated to the ED for patients with persistent tachycardia or vomiting.

Case Conclusions

CASE 1

For the 45-year-old man with fatigue, muscle cramps, and light-headedness who was taking lisinopril and semaglutide...

You considered that GLP-1 receptor agonists combined with angiotensin-converting enzyme (ACE) inhibitors reducing renal potassium excretion can lead to hyperkalemia. An electrocardiogram demonstrated peaked T-waves but no widening of the QRS. His serum potassium test resulted at 6.2 mmol/L, so you referred the patient to the ED immediately via EMS for treatment of hyperkalemia.

CASE 2

For the 38-year-old man with type 2 diabetes mellitus taking semaglutide experiencing nausea, vomiting, and epigastric discomfort...

You noted that nausea, vomiting, and abdominal pain are common side effects of GLP-1 receptor agonists but recognized that complications such as pancreatitis, electrolyte abnormalities, and gastroparesis are also on the differential. His laboratory test results, including a complete blood count, metabolic panel, and lipase, were negative for signs of metabolic acidosis or pancreatitis, and the patient felt better after receiving fluids and antiemetics. You discharged him with a prescription for ondansetron for nausea, given concern that speeding up gastric emptying would be counterproductive. You advised him to reduce or stop the medication, try smaller meals to help relieve symptoms, and to follow up with his primary care physician.

CASE 3

For the 29-year-old woman with a headache and hypertension after recent initiation of phentermine...

You noted that phentermine is a sympathomimetic appetite suppressant that can precipitate significant hypertension and tachycardia, especially during early treatment or for patients with a history of anxiety, which she reported. She had no chest pain, headache, visual changes, or shortness of breath, and her physical examination, including fundosocopy, was normal. An electrocardiogram showed sinus tachycardia but was otherwise normal, and laboratory testing revealed no end-organ damage. Her symptoms and blood pressure improved with supportive care of oral fluids and analgesics. Given the likely medication-related etiology of her symptoms, you advised her to stop taking the phentermine, avoid other stimulants (eg, caffeine, decongestants), and follow up with her primary care physician as soon as possible.

after reaching a goal. However, it is important to note that these microdoses are not FDA approved and lack clinical trial evidence supporting safety or effectiveness. Because weight loss from GLP-1 receptor agonist medications is generally dose-dependent, microdosing may lead to limited or inconsistent results. Safety concerns include the potential for medication to expire before it is fully used when patients extend the lifespan of a single pen or compounded vial.

Link to Euglycemic Ketoacidosis

Based on numerous case reports, there is growing concern for a link between GLP-1 receptor agonists and the occurrence of euglycemic DKA.[26-30] Data from the FDA Adverse Event Reporting System have also demonstrated a disproportionate number of DKA reports associated with GLP-1 receptor agonist use, with a proportional reporting ratio of 1.49.[31] The pathophysiology behind GLP-1 receptor agonists leading to euglycemic DKA is thought to be starvation and dehydration.[32] Patients with concurrent use of sodium-glucose cotransporter-2 (SGLT2) inhibitors are likely at even higher risk.[33] Given that laboratory findings of euglycemic DKA can mimic dehydration, a high index of suspicion is crucial to avoid missing this life-threatening condition.

Disposition

Evaluation in the ED is required for patients with evidence of severe dehydration, severe electrolyte disturbances, persistent nausea/vomiting, a concerning abdominal examination, or pancreatitis with uncontrolled symptoms. Hemodynamically stable patients with improved symptoms after supportive care and a reassuring abdominal examination can be discharged. Patients should follow up with their primary care provider and be provided with education about adverse effects of weight-loss medications and return precautions for worsening symptoms.

Summary

As the utilization of weight-loss medications continues to increase, UC clinicians will encounter a growing number of patients presenting with adverse effects related to these therapies. While GLP-1

Risk Management Pitfalls for Complications of Weight-Loss Medications in Urgent Care

1. **"Nausea is common in the setting of GLP-1 receptor agonist use, so I didn't think much of it."** While nausea is a common side effect of GLP-1 receptor agonist medications, persistent or worsening symptoms can signal gastroparesis or other complications. Monitor for progression and recommend follow-up care if symptoms do not improve with supportive measures.

2. **"I assumed that abdominal pain and vomiting was expected with GLP-1 receptor agonist use."** Persistent vomiting and abdominal pain in the epigastric region for patients taking GLP-1 receptor agonists should prompt evaluation for pancreatitis or other causes of abdominal pain such as cholecystitis. Careful physical examination can help guide evaluation. Always consider laboratory evaluation by checking serum lipase, as available, and consider referral to the ED for further assessment if clinical suspicion is high.

3. **"The patient reported abdominal pain and constipation, so I recommended a bowel regimen and sent them home."** GLP-1 receptor agonists can slow gastrointestinal motility, potentially leading to severe constipation or even bowel obstruction. Patients with significant abdominal pain, abnormal bowel sounds, or worsening symptoms may require ED evaluation for computed tomography imaging.

4. **"The patient mentioned muscle weakness, but we didn't obtain labs."** Hyperkalemia is a potential side effect of GLP-1 receptor agonists, particularly for patients with renal impairment or coexisting medication use (eg, ACE inhibitors). Electrolyte evaluation is essential for patients reporting nonspecific symptoms such as fatigue or weakness.

5. **"I assumed the abdominal pain was mild and related to GLP-1 receptor agonist use."** It is important to not attribute all types of abdominal discomfort solely to expected side effects of GLP-1 receptor agonist use. While patients using GLP-1 receptor agonists may develop appendicitis idiopathically, emerging evidence suggests a potential increased risk for appendicitis associated with these medications.[12] Patients with persistent, localized abdominal pain, particularly in the lower right quadrant, should be referred to the ED for advanced imaging to rule out appendicitis.

6. **"The patient had new neurological symptoms, but I didn't think their weight-loss med could be causing them."** Bupropion lowers the seizure threshold, making naltrexone-bupropion a higher-risk medication for patients with a history of seizures, eating disorders, or alcohol/benzodiazepine withdrawal.[2] Always ensure that a full medication history is taken, and recognize the risk for seizures with medications that include bupropion, especially for patients with other concurrent risk factors for seizure.

7. **"The patient taking phentermine-topiramate reported dizziness and palpitations, but I assumed it worked just like other weight-loss medications and was probably not related to the patient's symptoms."** Unlike GLP-1 receptor agonists, which primarily work through appetite suppression and delayed gastric emptying, phentermine is a stimulant that increases norepinephrine levels, which can elevate heart rate and blood pressure.[6] Dizziness and palpitations in these patients should prompt an evaluation for hypertension, arrhythmias, and cardiovascular risk factors, as continued use could exacerbate underlying conditions.

receptor agonists (eg, semaglutide, liraglutide, tirzepatide) have gained significant attention due to their efficacy in weight loss, other pharmacologic agents (eg, orlistat, phentermine-topiramate, and naltrexone-bupropion) are also widely prescribed. Each of these medications has a unique mechanism of action and potential complications that clinicians must recognize.

The most-reported adverse effects across these medications include gastrointestinal symptoms such as nausea, vomiting, diarrhea, and constipation. However, more serious complications have been observed, including pancreatitis, hyperkalemia, gallbladder disease, cardiovascular effects, psychiatric disturbances, and even appendicitis. Orlistat is associated with hepatic injury and severe gastrointestinal intolerance. Phentermine-containing medications may contribute to increased blood pressure and heart rate, while bupropion-based therapies lower the seizure threshold.

UC evaluation should focus on assessing the severity of symptoms, identifying any red-flag findings, and determining the need for escalation to emergency care. Patients presenting with severe abdominal pain, persistent vomiting, dehydration, altered mental status, significant electrolyte abnormalities, or hemodynamic instability should be referred for ED evaluation. In stable patients, supportive care remains the mainstay of treatment, including antiemetics, intravenous or oral hydration, electrolyte management, and symptom monitoring. Given the evolving landscape of obesity pharmacotherapy, continued clinical awareness and ongoing research will be essential in optimizing patient outcomes and ensuring safe prescribing practices.

■ Critical Appraisal of the Literature

A literature search was performed in PubMed, including the search terms *weight-loss medications, GLP-1 receptor agonist, orlistat, Xenical, phentermine-topiramate, Qsymia, naltrexone-burproprion, Contrave, liraglutide, Saxenda, semaglutide, Wegovy, setmelanotide, Imcivree, tirzepatide, Zepbound, emergency department, emergency medicine, primary care* and *urgent care* (alone and in combination) from the years 2000 to October 2024. This search yielded 115 results, most of which were deemed irrelevant to the workup or management of patients in the UC setting. The reference section of each article was reviewed for additional articles.

A search was also performed using the Cochrane Database of Systematic Reviews and Ovid MEDLINE® but yielded very limited information. The American Society for Metabolic and Bariatric Surgery guidelines were reviewed. In addition, many of the available articles were review articles, retrospective cohort studies, or case studies, with very few prospective randomized controlled trials. Clinical practice guidelines were published by the American College of Cardiology/American Heart Association in 2014[34] and clinical practice guidelines specific to pediatric patients were published in 2023 by the American Academy of Pediatrics.[4]

■ Time- and Cost-Effective Strategies

- Not all patients require intravenous fluid administration for mild dehydration. If the patient is able to tolerate liquids, then an oral rehydration fluid challenge may be administered in the clinic using commercial electrolyte solutions or popsicles.
- GLP-1 receptor agonist medications are commonly used for weight loss; however, many patients may not be familiar with the expected side effects. Some patients may have been prescribed these medications online without appropriate counseling on the expected effects of the medication. Consider creating handouts that your clinic may distribute to patients.
- Education on typical symptoms and side effects experienced with weight-loss medication use can be a good start to discharge instructions; however, be prepared to re-educate patients on the appropriate use of weight-loss medications and the expected side effects. Ensure that you are not minimizing potential serious adverse side effects such as persistent or severe abdominal pain, nausea, and vomiting that may indicate underlying pancreatitis or lactic acidosis.

■ References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study is included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

1. Yanovski SZ, Yanovski JA. Progress in pharmacotherapy for obesity. *JAMA*. 2021;326(2):129-130. **(Clinical review)**

2.* Yanovski SZ, Yanovski JA. Approach to obesity treatment in primary care: a review. *JAMA Intern Med*. 2024;184(7):818-829. **(Clinical review)** **DOI: 10.1001/jamainternmed.2023.8526**

3.* DeCleene NK, Kahn E, Yuan CW, et al. US state-level prevalence of adult obesity by race and ethnicity from 1990 to 2022 and forecasted to 2035. *JAMA*. 2026: e2526817. **(Survey data)** **DOI: 10.1001/jama.2025.26817**

4.* Hampl SE, Hassink SG, Skinner AC, et al. Clinical practice guideline for the evaluation and treatment of children and adolescents with obesity. *Pediatrics.* 2023;151(2):e2022060640. **(Practice guideline)** **DOI: 10.1542/peds.2022-060640**

5. Elangovan A, Shah R, Smith ZL. Pharmacotherapy for obesity-trends using a population level national database. *Obes Surg.* 2021;31(3):1105-1112. **(Prospective database study)**

6.* Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA.* 2014;311(1):74-86. **(Clinical review)** **DOI: 10.1001/jama.2013.281361**

7. Long B, Pelletier J, Koyfman A, et al. GLP-1 agonists: a review for emergency clinicians. *Am J Emerg Med.* 2024;78:89-94. **(Review)**

8.* Weghuber D, Barrett T, Barrientos-Perez M, et al. Once-weekly semaglutide in adolescents with obesity. *N Engl J Med.* 2022;387(24):2245-2257. **(Randomized controlled trial; 180 participants)** **DOI: 10.1056/NEJMoa2208601**

9. Knezevich E, Crnic T, Kershaw S, et al. Liraglutide-associated acute pancreatitis. *Am J Health Syst Pharm.* 2012;69(5):386-389. **(Case report)**

10. Hughes K, Sumaruth YRK, Mohammed E, et al. Acute pancreatitis likely due to semaglutide. *Cureus.* 2024;16(9):e69844. **(Case report)**

11. Fu EL, Wexler DJ, Cromer SJ, et al. SGLT-2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors and risk of hyperkalemia among people with type 2 diabetes in clinical practice: population-based cohort study. *BMJ.* 2024;385:e078483. **(Cohort study)**

12. Casella S, Galli K. Appendicitis: a hidden danger of GLP-1 receptor agonists? *J Pharm Technol.* 2024;40(2):108-111. **(Case report)**

13. Patel R, Wadid M, Makwana B, et al. GLP-1 receptor agonists among patients with overweight or obesity, diabetes, and HFpEF on SGLT2 inhibitors. *JACC Heart Fail.* 2024;12(11):1814-1826. **(Retrospective cohort study; 14,000 patients)**

14. 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;182(5):513-519. **(Meta-analysis; 76 randomized controlled trials, 103,371 patients)**

15. Wharton S, Davies M, Dicker D, et al. Managing the gastrointestinal side effects of GLP-1 receptor agonists in obesity: recommendations for clinical practice. *Postgrad Med.* 2022;134(1):14-19. **(Clinical review)**

16. Gentinetta S, Sottotetti F, Manuelli M, et al. Dietary recommendations for the management of gastrointestinal symptoms in patients treated with GLP-1 receptor agonist. *Diabetes Metab Syndr Obes.* 2024;17:4817-4824. **(Recommendations)**

17. Neeland IJ, Linge J, Birkenfeld AL. Changes in lean body mass with glucagon-like peptide-1-based therapies and mitigation strategies. *Diabetes Obes Metab.* 2024;26 Suppl 4:16-27. **(Review)**

18. Stefater-Richards MA, Jhe G, Zhang YJ. GLP-1 receptor agonists in pediatric and adolescent obesity. *Pediatrics.* 2025;155(4). **(Review)**

19. Pendrey A, Sevilla-Martir J. Antiobesity medications for older adults – the new, the good, the bad, and the unknown. *Obesity* (Silver Spring). 2025;33 (Suppl 1):57-73. **(Review)**

20. Novo Nordisk A/S. Ozempic® (semaglutide) full prescribing information. Bagsvaerd, Denmark: Novo Nordisk A/S; 2025. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2025/209637s025lbl.pdf **(Prescribing information)**

21. Kim DS, Latollari A, Khaimova R. Vitreous hemorrhage during GLP-1 receptor agonist treatment. *J Am Pharm Assoc.* 2023;63(3):976-979. **(Case report)**

22. Kindel TL, Wang AY, Wadhwa A, et al. Multisociety clinical practice guidance for the safe use of glucagon-like peptide-1 receptor agonists in the perioperative period. *Clin Gastroenterol Hepatol.* 2025;23(12):2083-2085. **(Clinical practice guidelines)**

23. United States Food & Drug Administration. "FDA's concerns with unapproved GLP-1 drugs used for weight loss." Updated February 4, 2026. Accessed March 15, 2026. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss **(Expert consensus)**

24. Berg S, Stickle H, Rose SJ, et al. Discontinuing glucagon-like peptide-1 receptor agonists and body habitus: a systematic review and meta-analysis. *Obes Rev.* 2025;26(8):e13929. **(Meta-analysis)**

25. Budini B, Luo S, Tam M, et al. Trajectory of weight regain after cessation of GLP-1 receptor agonists: a systematic review and nonlinear meta-regression. *medRxiv;* 2025. Preprint on June 9, 2025. Accessed on March 15, 2026. Available at: https://www.medrxiv.org/content/10.1101/2025.06.09.25328726v2 **(Systematic review)**

26. Kanu EO, Kim DK, Menon R, et al. Euglycemic ketoacidosis after the addition of glucagon-like peptide-1 receptor agonist: a case report. *Ann Intern Med Clin Cases.* 2024;3(6):e230565. **(Case report)**

27. Sood N, Bansal O, Garg R, et al. Euglycemic ketoacidosis from semaglutide in a patient without diabetes. *JCEM Case Rep.* 2024;2(9):luae156. **(Case report)**

28. Alduraibi RK, Alrebdi YM, Altowayan YF. Euglycemic diabetic ketoacidosis after the initiation of dulaglutide in patient with type 2 diabetes. *Medicine* (Baltimore). 2023;102(23):e34027. **(Case report)**

29. Zhang J, Ma Y, Zu Q, et al. GLP-1 receptor agonist-induced diabetic ketoacidosis: a case report. *Medicine* (Baltimore). 2024;103(39):e39799. **(Case report)**

30. Alghamdi M, Almulhim M, Alkhadra F, et al. A liraglutide injection superimposing a starvation acidosis: a case report. *Med Arch.* 2022;76(3):221-223. **(Case report)**

31. Yang Z, Yu M, Mei M, et al. The association between GLP-1 receptor agonist and diabetic ketoacidosis in the FDA Adverse Event Reporting System. *Nutr Metab Cardiovasc Dis.* 2022;32(2):504-510. **(FAERS database analysis)**

32. Patel N, Reddy A, Romero KN, et al. Euglycemic diabetic ketoacidosis in the setting of dulaglutide use. *Cureus.* 2025;17(4):e82143. **(Case report)**

33. Syed U, Fretes Oviedo NE, Variar V. 12621 convergence of SGLT2 inhibitors and GLP1 agonists: unveiling the recipe for euglycemic diabetic ketoacidosis. *J Endocr Soc.* 2024;8 (Supplement 1):bvae163.720. **(Case report)**

34. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association task force on practice guidelines and the obesity society. *J Am Coll Cardiol.* 2014;63(25 Pt B):2985-3023. **(Guidelines)**

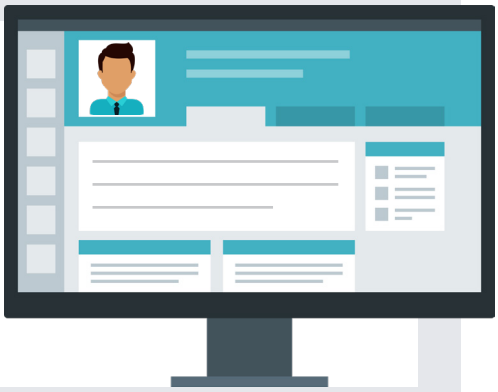
Coding & Charting: What You Need to Know

- A patient who presents with an adverse effect from a weight-loss medication will often have a chief complaint of nausea/vomiting, dehydration, constipation, or abdominal pain. A practical tip is to always code the condition being treated first; the adverse effect code (T50.995A – adverse effect of unspecified drug/medications, initial encounter) can be added later. The seventh character specifies whether the visit is the initial encounter (A), subsequent (D), or sequela (S). Most urgent care visits will use "A." When relevant, be sure to include BMI (Z68.xx) and obesity diagnosis (E66.9) to support medical necessity and context of treatment.
- Differentiate between an adverse effect versus poisoning. This matters significantly for compliance and audits. For example, if the patient took the medication correctly and developed side effects, the coding approach will be an adverse effect. Conversely, if the patient doubled their dose, that would be considered poisoning. GLP-1 receptor agonist overdosing (especially compounded semaglutide errors) should often be coded as poisoning if the drug is taken incorrectly.
- In your history and physical examination notes, clearly link the chief complaint to the medication. Document start date, dose, recent escalation, and timing of symptoms relative to injection or ingestion. Clear linkage will support adverse effect coding, medical decision-making (MDM) complexity, and justification for any laboratory testing, intravenous fluids, or prescription antiemetics.
- Weight-loss medication complications can mimic serious conditions. For example, if pancreatitis, bowel obstruction, or gallbladder disease are in the differential diagnosis, be sure to note what condition was considered, what conditions were ruled out, and why imaging or laboratory tests were or were not ordered. This strengthens risk-based coding. Clearly documented severity and risk of the patient's symptoms also support moderate or high medical-decision making. Signs of dehydration, inability to tolerate oral intake, imaging or intravenous fluids administered, or emergency department transfer affects E/M level selection. Be sure your documentation reflects prescription drug management, medication adjustment, and/or systemic symptoms.
- If appropriate, be sure to document injection site and dermatologic reactions such as location, size, warmth, systemic symptoms, and urticaria versus cellulitis versus allergic reaction.
- Support your disposition and follow-up with details about medication adjustment, prescription instructions, emergency department transfer (if needed), and clear return precautions.

Coding Challenge: Weight-Loss Medication Complications

By Bradley Laymon, PA-C, CPC, CEMC
Certified Physician Assistant, Winston-Salem, NC

A 38-year-old male patient presents as a new patient to the urgent care clinic with nausea, vomiting, and epigastric pain for the past 24 hours. He started semaglutide 6 weeks ago for weight loss. He reports progressive nausea over the past week, but today he has had multiple episodes of vomiting and upper abdominal pain. Pain is constant, located in the epigastric region, and rated 3 out of 10. He denies fever, chest pain, dyspnea, hematemesis, melena, diarrhea, hematochezia, dysuria, hematuria, flank pain, or dizziness.



PATIENT HISTORY
Past medical history: Type 2 diabetes mellitus, BMI 55 (morbid obesity)
Medications: Semaglutide 0.5 mg weekly subcutaneous injection; metformin 500 mg BID with food
Allergies: No known drug allergies

OBJECTIVE FINDINGS
BP: 122/76 mm Hg (right arm, sitting)
HR: 106 beats/min
RR: 16 breaths/min
Temp: 98.8°F
SpO_2: 99% on room air
Weight: 330 pounds
BMI: 55.9
General: Appears in minimal distress due to pain. He speaks in complete sentences with no accessory muscle use; alert and cooperative.

PHYSICAL EXAMINATION
Head: Normocephalic
Eyes: Conjunctiva clear, PERRLA
Ears: No papilledema, TMs clear
Nose/throat: Oropharynx is clear
Neck: Supple, no lymphadenopathy
Cardiovascular: Slightly tachycardic rate and rhythm, no murmur
Respiratory: Clear to auscultation bilaterally
Abdomen: Soft, nondistended, mild epigastric tenderness, no guarding or rebound, bowel sounds present in all quadrants
Rectal: No masses, no fissures, no gross blood
Skin: Warm and dry

LABORATORY STUDIES
CBC: To check for infection, anemia
CMP: To check for electrolyte abnormalities, liver function, and renal function
Lipase: To check pancreas function

IMPRESSION/PLAN
Assessment: Epigastric abdominal pain with nausea and vomiting; differential includes but is not limited to pancreatitis, semaglutide adverse effects, peptic ulcer disease, bowel obstruction, diverticulitis, irritable bowel syndrome, and appendicitis. Likely cause is an adverse effect to semaglutide. The others are unlikely based on history and examination findings.
Treatment plan: Prescription for ondansetron 4 mg TID PRN nausea provided. Semaglutide temporarily held pending lab results. Strict return precautions discussed including worsening pain, persistent vomiting, or signs of dehydration. Patient should follow up in 48 to 72 hours or sooner if symptoms worsen.

Abbreviations: BID, twice a day; BP, blood pressure; BMI, body mass index; CBC, complete blood count; CMP, comprehensive metabolic panel; HR, heart rate; PERRLA, pupils are equal, round, and reactive to light and accommodation; PRN, as needed; RR, respiratory rate; SpO_2, oxygen saturation of peripheral capillaries; temp, temperature; TID, 3 times a day; TMs, tympanic membranes.

Consider this patient encounter using the Simplified Elements of Medical Decision Making table provided in **Box 1**, then select the appropriate E/M code for this visit.

Number and Complexity of Problems Addressed
The patient presents with nausea, vomiting, and abdominal discomfort. Patient is tachycardic and in mild distress. This meets criteria for an acute illness with systemic symptoms, which is **Moderate, Level 4**.

Amount and/or Complexity of Data to be Reviewed and Analyzed
Three laboratory tests were ordered (CBC, CMP, lipase). This meets criteria for **Moderate, Level 4.**

Risk of Complications and/or Morbidity or Mortality of Patient Management
The patient was prescribed ondansetron. This meets the criteria for **Moderate, Level 4.**

ANSWER: Two of the 3 elements of MDM must be met when selecting the level of service. **Level 4** criteria were met in Problems Addressed, Complexity of Data, and the Risk of Patient Management. This visit supports **99204**.

Box 1. Simplified Elements of Medical Decision Making

MDM Level*	Problems Addressed	Complexity of Data	Risk of Patient Management	E/M Service Codes
Level 2: Straightforward	• Minor/self-limited	• Minimal/none	• Minimal risk of morbidity	• 99202 (new) • 99212 (established)
Level 3: Low	• ≥1 minor/self-limited problem • 1 stable chronic illness • 1 acute, uncomplicated illness • 1 acute, uncomplicated injury	At least 1 of these: • 2 data sources (eg, ordering or reviewing tests) • Independent historian	• Low risk of morbidity • Example: Over-the-counter medication management	• 99203 (new) • 99213 (established)
Level 4: Moderate	• ≥1 chronic illnesses with exacerbation/progression/ treatment side effects • 1 acute, complicated injury • ≥2 stable chronic illnesses • 1 undiagnosed new problem • 1 acute illness with systemic symptoms	At least 1 of these: • 3 data sources (eg, ordering or reviewing tests); can include independent historian • Independent interpretation of test results • Discussion of management or test interpretation	• Moderate risk of morbidity • Examples: Prescription drug management; significant social determinants of health; decision regarding escalation of care	• 99204 (new) • 99214 (established)
Level 5: High	• ≥1 chronic illnesses with **severe** exacerbation/ progression/treatment side effects • Illness or injury that threatens life or bodily function	At least 2 of these: • 3 data sources (eg, ordering or reviewing tests); can include independent historian • Independent interpretation of test results • Discussion of management or test interpretation	• High risk/severe without emergent treatment	• 99205 (new) • 99215 (established)

*Level is determined by meeting or exceeding 2 out of 3 elements of medical decision making.
Abbreviations: E/M, evaluation and management; MDM, medical decision making.
Based on data from: American Medical Association. *Evaluation and Management (E/M) Services Guidelines,* 2023.

■ CME Questions

Current *Evidence-Based Urgent Care* subscribers receive CME credit absolutely free by completing the following test. Each issue includes 4 *AMA PRA Category 1 Credits™*. To receive CME credits for this issue, scan the QR code below with an enabled mobile device or visit https://www.ebmedicine.net/UC0426

1. **What is the first step in the management of a patient with a potential weight-loss medication side effect?**
   a. Ordering laboratory testing
   b. Obtaining a detailed history and physical examination
   c. Referring the patient to the emergency department (ED)
   d. Administering IV fluids

2. **Which of the following symptoms is the most common side effect associated with the use of GLP-1 receptor agonists?**
   a. Nausea
   b. Lactic acidosis
   c. Arrhythmia
   d. Wheezing

3. **Which of the following is a reasonable approach to management of a patient experiencing mild nausea while taking a GLP-1 receptor agonist medication?**
   a. Immediate referral to the ED
   b. Initiation of proton pump inhibitor medication
   c. Treatment with an antiemetic (avoiding metoclopramide) and dietary counseling
   d. Discontinuation of the GLP-1 medication without having patient talk to their primary care physician

4. **Which of the following is NOT a red-flag symptom that warrants ED referral?**
   a. Severe epigastric abdominal pain
   b. Intractable vomiting
   c. Syncope
   d. 1 day of constipation without vomiting

5. **Which medication works by increasing norepinephrine release, leading to appetite suppression-modulation of GABA activity?**
   a. Phentermine
   b. Semaglutide
   c. Orlistat
   d. Sulfonylurea

6. **Which of the following is not a commonly used class of weight-loss medication?**
   a. GLP-1 receptor agonists
   b. Dual GIP/GLP-1 receptor agonist
   c. Alpha-receptor agonists
   d. Pancreatic lipase inhibitors

7. **What is an important consideration when evaluating patients using stimulant-type weight-loss medications?**
   a. Evaluate for weight loss
   b. Consider cardiovascular side effects
   c. Initiate concurrent GLP-1 receptor agonist medication use
   d. Initiate intravenous fluids

8. **Which weight-loss medication can cause neurological side effects such as lowering seizure threshold?**
   a. Semaglutide
   b. Phentermine
   c. Orlistat
   d. Naltrexone-bupropion

9. **Which electrolyte abnormality is a potential side effect of GLP-1 receptor agonist use, especially for patients with concurrent angiotensin-converting enzyme-inhibitor use?**
   a. Hypocalcemia
   b. Hypomagnesemia
   c. Hyperkalemia
   d. Hypernatremia

10. **Which of the following is a potential symptom of hyperkalemia?**
    a. Muscle weakness
    b. Dry mucous membranes
    c. Blurry vision
    d. Hypertension

EB MEDICINE

Direct all inquiries to:
Phone: 678-366-7933
Fax: 770-500-1316
5600 Spalding Drive, Unit 921697
Norcross, GA 30010-1697
E-mail: ebm@ebmedicine.net
Website: www.ebmedicine.net

Chief Executive Officer: Stephanie Williford
Director of Operations: Robin Wilkinson
VP of Publishing: Suzanne Verity
VP of Marketing & Technology: Anna Motuz, MBA
Senior Content Editor: Cheryl Belton, PhD, ELS
Senior Content Editor: Anneke Smith, MS
Managing Editor/Product Development: Angie Wallace
CME & Content Manager: Kristen Raynor, MEd
Associate Content Editor: Lindsay Petracek
Senior Account Executive: Dana Stenzel
Database Administrator: Jose Porras
Conversion Optimization Specialist: Saylor Green
Marketing Coordinator: Stephanie Allen
Marketing Coordinator: Becky Smith
Marketing Specialist: Valerie Yuhouse
Account Executive: Jack Dugan
Client Success Manager: Kandis Slater
Customer Service Representative: Katie Resumovic

ISSN info and disclaimer:

Evidence-Based Urgent Care (ISSN Online: 2833-7565) is published by EB Medicine (5600 Spalding Drive, Unit 921697, Norcross, GA 30010-1697).