PRACTICE AID

Overview of Indications and Dosing Frequency for Approved GLP-1 RA and GIP/GLP-1 RA Agents

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/YWP40**

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Agents for T2DM	Indications				
	Dosing frequency	Adjunct to diet and exercise to improve glycemic control in adults with T2DM	Adjunct to diet and exercise to improve glycemic control in patients aged ≥10 with T2DM	Reduce risk of MACE in adults with T2DM and established CVD	Reduce risk of MACE in adults with T2DM and multiple CV risk factors
Dulaglutide (Trulicity)[1]	Once weekly SC	Yes	Yes	Yes	Yes
Exenatide (Byetta)[2]	Twice daily SC	Yes	–	–	–
Exenatide ER (Bydureon BCise)[3]	Once weekly SC	Yes	Yes	–	–
Liraglutide (Victoza)[4]	Daily SC	Yes	Yes	–	–
Lixisenatide (Adlyxin)[5]	Daily SC	Yes	–	–	–
Semaglutide (Ozempic)[6]	Once weekly SC	Yes	–	Yes	–
Semaglutide (Rybelsus)[7]	Daily oral	Yes	–	–	–
Tirzepatide (Mounjaro)[8]	Once weekly SC	Yes	–	–	–

1. Trulicity (dulaglutide) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125469s051lbl.pdf. 2. Byetta (exenatide) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/021773s048lbl.pdf. 3. Bydureon BCise (exenatide ER) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/209210s023lbl.pdf. 4. Victoza (liraglutide) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/022341s039lbl.pdf. 5. Adlyxin (lixisenatide) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208471s007lbl.pdf. 6. Ozempic (semaglutide) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/209637s020s021lbl.pdf. 7. Rybelsus (semaglutide) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213051s018lbl.pdf. 8. Mounjaro (tirzepatide) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215866Orig1s002s006lbl.pdf.

PRACTICE AID

Applying the "3Es" to Manage GI Adverse Events of GLP-1 RAs[1]

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/YWP40**

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The First Es: Education/Explanation and Escalation

Education and Explanation

Patient consultation and counseling

- Counsel patients on
  - The potential for GI AEs and their typically mild-to-moderate, temporary nature
  - Dietary modifications: recommend reducing meal size, being mindful to stop eating once full, avoiding eating when not hungry, avoiding high-fat or spicy food, and moderating alcohol intake
- Discuss any current GI symptoms, treat if needed, and counsel the patient on how to manage any potential worsening symptoms after GLP-1 RA initiation

Escalation to an Appropriate Dose

Initiation with gradual dose escalation

- Follow the gradual dose escalation strategy recommended in the GLP-1 RA prescribing information
- Consider slower dose escalation for patients reporting challenges with GI symptoms in the first few weeks of treatment

If patient presents with GI adverse events … (continued next page)

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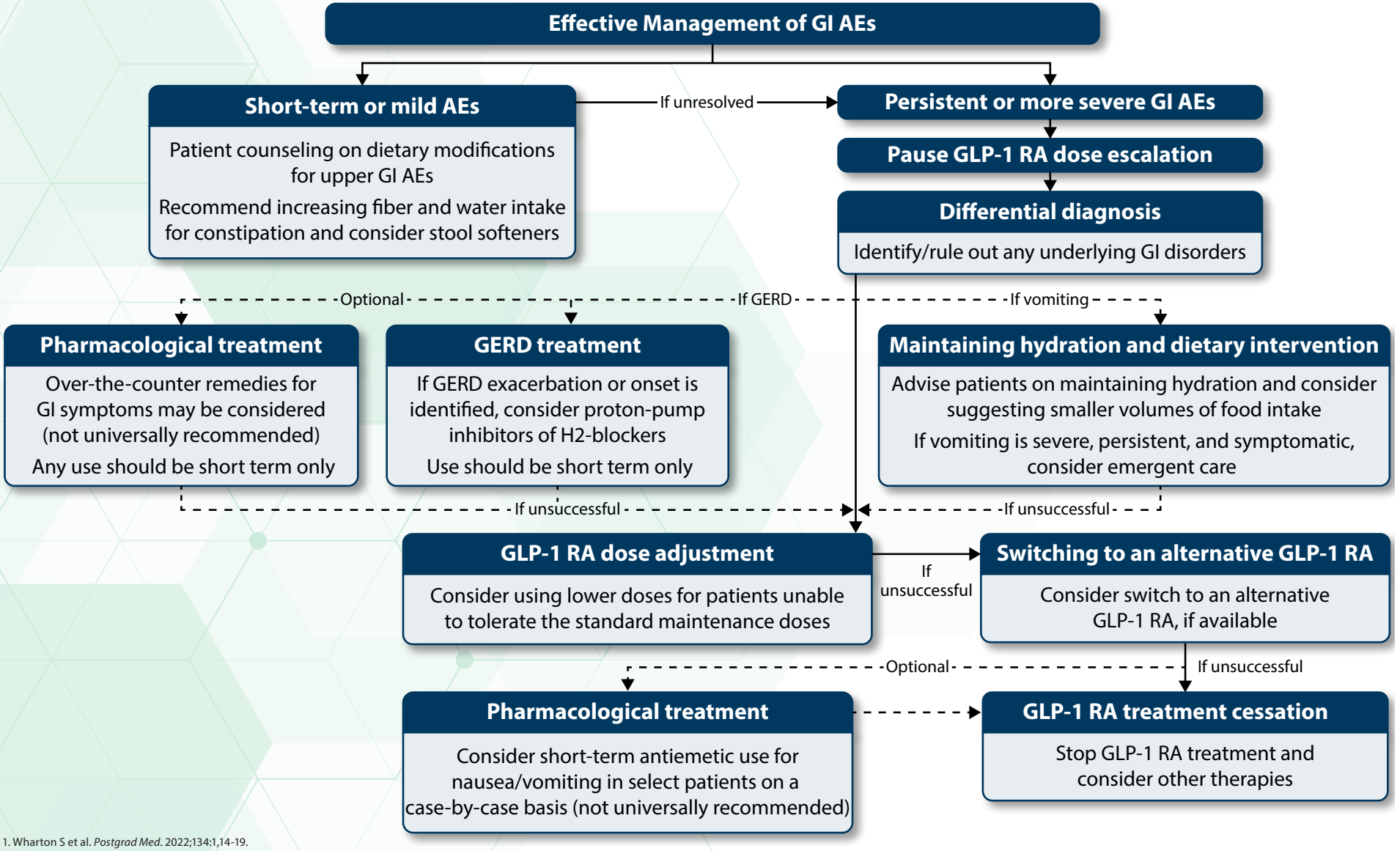
The Final E: Effective Management



1. Wharton S et al. *Postgrad Med*. 2022;134:1,14-19.

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Overview of Indications and Dosing Frequency for Approved GLP-1 RAs[1]

PeerView Primary Care

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GLP-1 RA Shortage Strategies: Comparative Doses for Interchanging GLP-1 RA Therapies or Extended Interval Dosing

In the case of drug shortages or drug switching, clinicians should know the comparative doses for interchanging GLP-1 RAs as well as how to administer intermediate doses of semaglutide for slower dose uptitration

GLP-1 RAs, GIP/GLP-1 RA for Diabetes Treatment

Agent	Dosing Interval	Comparative Doses									
Exenatide	SC twice daily	5 mcg[a]	10 mcg	–	–	–	–	–	–	–	–
Lixisenatide	SC daily	10 mg[a]	20 mg	–	–	–	–	–	–	–	–
Liraglutide	SC daily	0.6 mg[a]	1.2 mg	1.8 mg	–	–	–	–	–	–	–
Exenatide XR	SC weekly	–	–	2 mg	–	–	–	–	–	–	–
Dulaglutide	SC weekly	–	0.75 mg[a]	1.5 mg	3 mg	4.5 mg	–	–	–	–	–
Semaglutide	SC weekly	–	0.25 mg[a]	0.5 mg	–	1 mg	2 mg	–	–	–	–
Semaglutide	PO daily	3 mg[a]	7 mg	14 mg	–	–	–	–	–	–	–
Tirzepatide	SC weekly	–	–	2.5 mg[a]	–	–	5 mg	7.5 mg	10 mg	12.5 mg	15 mg

Alternative Intermediate Doses of Injectable Semaglutide

Semaglutide Pen (Product Concentration)	Weekly Semaglutide Intermediate Doses					
0.25 and 0.5 mg (2 mg/3 mL)[b]	0.5 mg	0.4 mg	0.33 mg	0.25 mg	0.12 mg	0.06 mg
1 mg (4 mg/3 mL)	1 mg	0.8 mg	0.66 mg	0.5 mg	0.25 mg	0.12 mg
2 mg (8 mg/3 mL)	2 mg	1.6 mg	1.33 mg	1 mg	0.5 mg	0.25 mg
Number of clicks for desired intermediate dose	74	59	49	37	18	9
Number of available weekly doses using an intermediate dose	4	5	6	8	8[c]	8[c]

[a] Comparative efficacy of starting doses is not known; these figures are based on expert opinion. [b] New semaglutide pen concentration as of March 2023; doses not confirmed by the manufacturer but rather mathematically calculated by the authors. [c] Injected semaglutide is stable for 56 days (8 weeks) once opened and should be discarded thereafter.

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Overview of Indications and Dosing Frequency for Approved GLP-1 RAs[1]

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Manufacturer Recommendations for Missed Doses of GLP-1 RAs

Agent	Recommended Dosing Interval	Manufacturer Recommendations for Missed Doses
Short-acting agents		
Exenatide	Twice daily	• Skip missed dose and resume at the next scheduled dose
Lixisenatide	Once daily	• If a dose is missed, administer within 1 hour prior to next meal
Long-acting agents		
Dulaglutide	Once weekly	• Administer as soon as possible if there are ≥3 days (72 hours) until next scheduled dose • If <3 days before next scheduled dose, skip the missed dose and administer on the next scheduled day
Exenatide XR	Once weekly	• Administer as soon as possible if there are ≥3 days (72 hours) until next scheduled dose • If <3 days before next scheduled dose, skip the missed dose and administer on the next scheduled day
Liraglutide	Once daily	• If a dose is missed, resume with the next scheduled dose
Semaglutide (injectable)	Once weekly	• Administer as soon as possible within 5 days after the missed dose • If >5 days have passed, skip the dose and administer on the next scheduled day
Semaglutide (oral)	Once daily	• If a dose is missed, resume with the next scheduled dose
Tirzepatide	Once weekly	• Administer as soon as possible within 4 days (96 hours) after the missed dose • If >4 days have passed, skip the dose and administer on the next scheduled day

1. Whitley HP et al. *Clin Diabetes*. 2023;41:467-473.

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Speaking to Patients About GLP-1 RAs[1]

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1 Before

Save time to speak with the patient

- Convey realistic expectations regarding treatment results
- Inform about GI effects, pointing out that they will soon pass
- Highlight the importance of following the available guidelines

2 Dose Escalation

If GI AEs occur, **slow down** the planned dose increments to reach success

Strategies for slower dose escalation

- Extend phase for 2-4 more weeks before moving forward to next dose
- Suspend treatment temporarily
- If GI AEs appear just after escalation, go back to prior dose for a few days, then increase dose gradually
- If problem persists, consider setting up as maintenance therapy a dose lower than the maximum one

3 Dose Escalation or Maintenance Phase

If GI AEs persist beyond normal in time/severity, **implement additional** measures

Strategies for dealing with persistent or severe GI AEs

- Consider the differential diagnosis to rule out
- Reinforce dietary and lifestyle guidance
- Start measures specifically focused on the troublesome symptoms
  - Additional patient guidelines (provided on next page)
  - Pharmacological support can be considered (short-term use only)

Nausea
- Antiemetics
- Prokinetics (domperidone)

Vomiting
- Antiemetics
- Prokinetics (domperidone)
- Standard procedures for severe cases (do not rule out IV rehydration)

Diarrhea
- Probiotics
- Antidiarrheals (loperamide)
- Consider metformin dose reduction when needed

Constipation
- Stool softeners
- Consider reducing GLP-1 RA dose

Print the following page about healthy habits and adverse events and share with your patients when prescribing a GLP-1 RA

1. Gorgojo-Martínez JJ et al. *J Clin Med*. 2022;12:145.

Healthy Habits to Address Potential Gastrointestinal Effects of GLP-1 Receptor Agonists (RAs)

Healthy Habits

1 Eating Habits

Eat slowly

Eat only **if really** hungry

Smaller portions

No lying down **after meal**

Stop **when** full

Smaller, more frequent meals

No **straw**

No distractions, enjoy **savoring**

Not too active **after meal**

No meals **near bedtime**

2 Food composition and preparation

- Low-fat **diet**
- **Boil**, bake, roast, griddle
- **Clear drinks** (small sips, not too much)
- Water-rich **foods**

3 Lifestyle

- **Fresh air**, light exercise
- Food diary to identify **what works better**
- **Mindful eating**

What to Know About Potential Side Effects

Nausea

- Eat crackers, apples, mint, ginger-based drinks
- Avoid strong smells

Vomiting

- Generous **hydration**
- More frequent meals **in smaller amounts**

Constipation

- **Enough** fiber in diet
- **Increase** physical activity
- **Healthy** balanced diet
- **Generous hydration** (water, sugar-free liquids)

Diarrhea

- **Generous hydration** (water, lemon)
- **No high fiber content foods** (gradually restore them upon improvement)
- **Yes:** chicken broth, rice, carrots, ripe peeled fruit, baked fruit
- **Minimize:** dairy products, laxatives, coffee, alcohol, soft drinks, very cold/hot foods, products with sweeteners ending in "-ol"

In case of severe/persistent nausea/vomiting, no drinks during meals; take drinks 30-60 minutes before and/or after meals

Should any GI effects be severe/persistent in spite of following all guidelines, contact HCP as soon as possible