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Pharmacy Pearls

GLP-1 RAs for Weight Loss

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General Considerations for Weight Loss Drugs

- Consider for patients with BMI ≤30 or BMI ≤27 with ≥1 weight-related comorbidity (e.g., HTN, T2DM, HLD)
- Pharmacotherapy should be viewed as adjunct to diet/lifestyle modifications as opposed to stand-alone treatment
- Loss of ≥5% of body weight is considered clinically significant
- Consider discontinuing treatment if clinically significant weight loss is not achieved after 12-16 weeks of full-dose therapy

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists (RAs) for Weight Loss

Weight loss has been observed with all GLP-1 RAs, but certain agents in the class have demonstrated a more pronounced effect than others. This may be due to higher dose regimens and/or drug-specific characteristics.

Average Weight Loss with GLP-1 RAs

Drug	Absolute Change in Body Weight*
Exenatide (Bydureon®) 2 mg	-1.6%
Dulaglutide (Trulicity®) 1.5 mg	-2.2%
Dulaglutide (Trulicity®) 4.5 mg	-4.4%
Liraglutide (Victoza®) 1.8 mg	-2.5%
Liraglutide (Saxenda®) 3 mg^	-5.5%
Semaglutide (Ozempic®) 1 mg	-6.2%
Semaglutide (Wegovy™) 2.4 mg^	-12.5%

*Defined as mean loss in treatment group – mean loss in placebo group
^FDA approved for weight loss

Semaglutide (Wegovy™) is the second GLP-1 RA to receive an indication for weight loss; liraglutide (Saxenda®) was the first. Wegovy™ contains the same medication as Ozempic® and Rybelsus® (semaglutide), but in a higher dose, and is the first medication approved for chronic weight management in adults since 2014.

The Data - High Dose Semaglutide for Weight Loss

- Population: >1900 non-diabetic adults, BMI ≥30 kg/m2 or ≥27 kg/m2 with at least one weight-related comorbidity, ~75% white females, average age 46.5 years, mean baseline weight 105 kg, mean baseline BMI ≥38 kg/m2
- After 68 weeks, patients who took semaglutide lost an average of 14.9% of their body weight vs. 2.4% of patients taking placebo
    - Nearly 35% of patients taking semaglutide lost ≥20% of their body weight vs. 2% of patients taking placebo
- GI complaints were commonly reported in both groups (72% of treatment and 48% of placebo patients)
- Hypoglycemia was reported in 0.6% of treatment and 0.8% of placebo patients
- Gallbladder disorders occurred in 2.6% of patients taking semaglutide and 1.8% of patients taking placebo (potentially related to the degree of weight loss observed)
- There were 3 cases of acute pancreatitis in the treatment group and no cases in the placebo group; all cases occurred in patients with a history of pancreatitis

Comparison of Select Weight Loss Agents

Drug	Absolute Change in Body Weight*	Adverse Effects	Other Considerations
Orlistat (Alli®, Xenical®)	-2.0 – 4.0%	• GI discomfort, bloating, flatulence • Fecal urgency or incontinence • Nephrolithiasis • Liver injury (rare) *GI side effects can be minimized with a low-fat diet*	• Reduces absorption of fat-soluble vitamins; patient will require MVI with vitamins A, D, E, K • Take other medications ≥1 hour before or 2 hours after orlistat • Avoid in patients with malabsorption syndromes, kidney stones, or cholestasis
Naltrexone/bupropion (Contrave®)	-4.1%	• Anxiety • Insomnia • Nausea • Constipation • Headache	• Bupropion may be overly stimulating for patients with anxiety • Bupropion lowers seizure threshold- avoid in at-risk patients • Naltrexone cannot be used in patients on chronic opioid therapy • Avoid in patients with uncontrolled HTN
Phentermine/topiramate (Qsymia®) **-Low dose (3.75 mg/23 mg)** **-High dose (15 mg/92 mg)**	 -3.5% -9.4%	<u>Phentermine</u> • ↑BP/HR • Anxiety • Insomnia • Dry mouth • Constipation <u>Topiramate</u> • Paresthesia • Cognitive/memory impairment • Nephrolithiasis • Dizziness • ↓serum bicarbonate	• Only available through REMs certified pharmacies • Caution in patients with seizure risk, tachyarrhythmias, anxiety, insomnia, or h/o kidney stones • Risk of hyperchloremic non-anion gap metabolic acidosis highest in patients with renal impairment, diarrhea, or ketogenic diets
Liraglutide (Saxenda®)	-4.5%	• Nausea • Vomiting • Constipation or diarrhea • Cholelithiasis, cholecystitis *GI side effects can be minimized with slow dose titration and should improve over time*	• Shown to reduce risk of CV events in DM patients with ASCVD • AKI has been reported secondary to volume loss due to GI adverse effects • Caution in patients with h/o pancreatitis • Avoid in patients with personal or family h/o medullary thyroid carcinoma
Semaglutide (Wegovy™)	-12.4%		

*Defined as mean loss in treatment group – mean loss in placebo group