AGA Clinical Practice Guideline on Pharmacological Interventions for Adults with Obesity

By Chuma Obineme

@EmoryGastroHep

In adults with BMI ≥30kg/m² or ≥27kg/m² and weight related complications who have an inadequate response to lifestyle interventions, the AGA recommends the addition of pharmacologic anti-obesity medications (AOM's) to lifestyle interventions over lifestyle interventions alone.

Conditional Recommendation, Moderate Evidence: **Semaglutide, Liraglutaide, Phentermine-Topiramate ER, and Naltrexone Bupropion ER**

Conditional Recommendation, Low Evidence: Phentermine and Diethylpropion (FDA approved for 12wks, avoid in CVD and HTN)

Key Pharmacologic Considerations

- Presence of relevant comorbidities
- Age/Gender
- Adverse side effects
- Childbearing age
- % Total body weight loss (TBWL) desired
- Cost
- Access
- Chronicity of obesity

Absolute/Relative Contraindications for all AOM's

- **AOM's should not be used in pregnant women**
- **They should be avoided in patients with bulimia nervosa**
- Decline in weight may be accompanied by decreases in blood pressure and blood glucose which requires ↑ monitoring

Drug	Mechanism of Action	Favorable Comorbidities	%TBWL	Monitoring/Drug Titration	Adverse Effects	Contraindications
Semaglutide 2.4mg (SQ inj weekly dosing; Oral dosing not FDA approved for obesity)	•GLP-1 Receptor agonist; endogenous incretin hormone produced by L cells in the intestinal mucosa •Glucoregulatory benefits	Type 2 Diabetes Mellitus (T2DM)	**10.46%**	Slow dose titrated dose escalation from 0.25mg → 2.4 (over 16 weeks) Decreases adverse effects	•Increased risk of pancreatitis and gallbladder disease •Delays gastric emptying, increased N/V •BG monitoring due moderate increased risk of hypoglycemia	•Contraindicated in patients with a personal or fam hx of **Medullary thyroid cancer or Multiple Neuroendocrine Neoplasia 2 (MEN2)** •Should not be used with another GLP1 RA, or DPP 4 inhibitors
Liraglutide. 3.0mg (Daily SQ inj)			**4.8%**	Slow titrated dose escalation 0.6mg → 3.0mg (over 4-6 wks); less side effects		

Co-management with Endocrinology or Obesity Medicine certification is strongly encouraged for providers prescribing these drugs.

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Drug	Mechanism of Action	Favorable Comorbidities	% TBWL	Monitoring/Drug Titration	Adverse Effects	Contraindications (Relative and Absolute)
Phentermine-Topiramate ER (15mg/92mg) *Schedule IV controlled substance*	•Phentermine – Monoamine sympathomimetic (elevated NE) •Topiramate - unknown GABA-R modulation	**Migraine headaches**	**8.45%**	Slow titrated dose escalation 3.75mg/23mg →15mg/92mg Monitor BP	•Insomnia, cognitive impairment, constipation, dry mouth, palpitations, paresthesia's, irritability, dysgeusia	•Agent is **Teratogenic**; Childbearing age female pts need contraception •**Avoid in those with CVD or uncontrolled HTN** •Avoid in those taking **MAOI's**
Naltrexone-Bupropion ER (8mg/90mg)	•Naltrexone – Opioid antagonist •Bupropion – Dopamine and NE reuptake inhibitor	**Depression** **Tobacco use**	**3.01%**	BP & HR monitored during first 12 weeks of therapy. Start 1tab qD → 2tabs BID	•Nausea, vomiting, headache, dizziness depression	•Avoid in patients with **seizure** disorders or patients at high risk for seizures. •Should not be **concomitantly used with opioid medications** •Hepatically metabolized, caution in **liver disease**
Orlistat 120mg (AGA recommends ***against*** the use of this agent)	•Long-acting irreversible inhibitor of G.I. lipase, prevent fat digestion		**2.78%**	Therapy should be ingested at least 1 hour within eating a meal; TID dosing Monitor and supplement Vitamin A, D, E and K	•Low levels of Vitamin A,D, E, and K; take supp •Flatulence, oily spotting/stools, fecal urgency and fecal incontinence	•Mild increased risk of cholelithiasis •Patients with a malabsorptive syndromes (i.e. celiac disease, IBD, bariatric surg) are likely poor candidates for long term tx
Gelesis 100 (No recommendation)	•Oral super absorbent hydrogel expands in stomach	**T2DM**	**2.02%**	Unclear, knowledge gap	•Small studies, but SAEs were similar to control group	•No current absolute contraindications, current knowledge gap

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