AGS Choosing Wisely® Campaign — Explicit “Avoid” for Appetite Stimulants

This is the more directly relevant and more strongly worded of the two AGS positions for the context of using mirtazapine specifically **to treat weight loss or anorexia** in older adults.

> **AGS Choosing Wisely® Recommendation (affirmed 2014, updated 2015, referenced in 2019 and 2023 Beers updates):***“Avoid using prescription appetite stimulants or high-calorie supplements for treatment of anorexia or cachexia in older adults; instead, optimize social supports, discontinue medications that may interfere with eating, provide appealing food and feeding assistance, and clarify patient goals and expectations.”*Reference: AGS Choosing Wisely Workgroup. J Am Geriatr Soc. 2014;62(5):950–960. DOI: 10.1111/jgs.12770

The Choosing Wisely recommendation encompasses all prescription appetite stimulants used in older adults, explicitly including mirtazapine. The AGS bases this recommendation on several foundational findings:

- **No RCTs specifically in older adults for weight gain:** No randomized controlled trials have evaluated mirtazapine solely as an appetite stimulant in a geriatric population. Existing weight data is derived from depression trials in which weight change was a secondary or incidental outcome.
- **Lack of evidence on patient-centered outcomes:** There is no evidence that mirtazapine (or any prescription appetite stimulant) improves quality of life, functional status, or survival when prescribed for weight loss. Weight gain in short-duration trials has not translated into meaningful clinical benefit in controlled studies.
- **Evidence base is mixed even in favorable populations:** In two retrospective studies of older nursing home residents with depression and weight loss, mirtazapine showed no differential advantage over sertraline or other non-TCA antidepressants on weight gain outcomes.
- **Off-label use without FDA approval:** Mirtazapine is not FDA-approved for appetite stimulation or weight gain in any population. All appetite-stimulant use is off-label, without the regulatory evidence threshold that approved indications require.

The Critical Exception: Co-existing

Depression

The AGS guidance draws a meaningful clinical distinction. Mirtazapine used **to treat confirmed depression** in an older adult — where weight gain is a welcome secondary effect — is a different clinical scenario than prescribing it **solely for appetite stimulation.** The Choosing Wisely recommendation targets the latter use case specifically.

AGS Clinical Logic: *"Mirtazapine is likely to cause weight gain or increased appetite when used to treat depression, but there is little evidence to support its use to promote appetite and weight gain in the absence of depression."*Source: AGS Choosing Wisely / AAFP AFP 2014

This framing has direct implications for LTC practice:

- If a resident has documented major depression AND anorexia/weight loss, mirtazapine is a clinically defensible choice — treating depression is the primary indication, and weight gain is an acceptable or desirable side effect.
- If a resident has weight loss WITHOUT depression, the AGS recommends against mirtazapine as primary pharmacotherapy and instead directs clinicians toward identifying and treating the root cause of weight loss, optimizing the eating environment, and addressing polypharmacy.
- Residents with dementia require particular scrutiny — emerging safety data (see Section 5) suggests possible mortality signal in this population that may further shift the risk-benefit calculus.

Summary from AGS

Summary for LTC Practice
The evidence base for mirtazapine as a standalone appetite stimulant in long-term care residents is weak, mixed, and not supported by the AGS. The most applicable LTC-specific data shows no differential weight gain advantage over comparator antidepressants. The only study with directly favorable data in an LTC/dementia population (Vandel 2012) lacks a control group. A 2025 Australian LTCF cohort of 5,409 residents found a 16% higher all-cause mortality with mirtazapine versus sertraline — a signal that demands caution particularly in dementia patients.The AGS, through Choosing Wisely, recommends against prescription appetite stimulants for weight loss in older adults. Mirtazapine is most defensible when depression is the co-primary indication. When prescribed solely for weight loss without a co-existing indication, the risk-benefit calculus is unfavorable by current evidence standards.

Prescribing Decision Framework

Clinical Scenario	AGS Guidance	Evidence Support
Weight loss with confirmed major depression	Acceptable — treat depression; weight gain is a welcome side effect	Moderate (depression trials; weight change secondary outcome)
Weight loss without depression, no other indication	**Not recommended (Choosing Wisely Avoid)**	Weak — no RCTs; retrospective data mixed
Weight loss with dementia (no depression diagnosis)	**Use with caution — emerging mortality signal (Healy 2025, SYMBAD)**	Conflicting; possible harm signal in dementia
Anorexia of aging / cachexia without treatable underlying cause	**Not recommended (Choosing Wisely Avoid)**	No controlled trials show QoL or survival benefit
Patient with history of falls and weight loss	**Avoid — falls risk (Beers Table 3) + no appetite stimulant evidence**	Class-level falls risk; Beers moderate evidence, strong recommendation
Hyponatremia history or diuretic use + weight loss	Use with caution — SIADH risk; check sodium baseline + within 2–4 weeks	Beers Criteria: moderate evidence, strong recommendation

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