CHOLINESTERASE INHIBITOR

Galantamine

Razadyne, Razadyne ER (formerly Reminyl)

Reversible cholinesterase inhibitor that also allosterically potentiates nicotinic receptors, approved for mild to moderate Alzheimer dementia.

USUAL ADULT DOSE	HALF-LIFE	METABOLISM	ONSET
16-24 mg/day PO	About 7 h	CYP2D6 and CYP3A4	Benefit judged at 3-6 months

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved only for mild to moderate dementia of the Alzheimer type, as immediate-release tablets or solution twice daily or extended-release capsules once daily.
- Efficacy is comparable to donepezil and rivastigmine, giving roughly a 2-3 point ADAS-cog advantage over placebo across 6-month trials.
- Should not be used for mild cognitive impairment, where two randomized trials found an unexplained excess of deaths in treated patients.
- Not approved for severe Alzheimer disease, vascular dementia, Parkinson disease dementia or dementia with Lewy bodies.
- Sometimes used off-label in mixed Alzheimer and vascular dementia, where trial results have been inconsistent and benefit is uncertain.
- May be combined with memantine in moderate disease, although the combination evidence is stronger for donepezil than for galantamine.

DOSING & TITRATION

- Immediate release: **4 mg** twice daily for 4 weeks, then 8 mg twice daily for at least 4 weeks, then 12 mg twice daily if needed and tolerated.
- Extended release: **8 mg** once every morning for 4 weeks, then 16 mg daily for at least 4 weeks, then 24 mg daily as the maximum dose.
- The effective maintenance range is **16-24 mg/day**; do not shorten the 4-week interval between steps, since that is what generates nausea.
- Take with food and adequate fluid, and if treatment is interrupted for several days, restart at the lowest dose and re-titrate upward.
- Moderate hepatic impairment (Child-Pugh 7-9) or creatinine clearance of 9-59 mL/min caps the dose at **16 mg/day**.
- Avoid entirely in severe hepatic impairment (Child-Pugh 10-15) or when creatinine clearance is below 9 mL/min.

MECHANISM OF ACTION

- Competitive and reversible inhibitor of acetylcholinesterase, raising synaptic acetylcholine in cortical and hippocampal circuits.
- Uniquely acts as an allosteric potentiating modulator at nicotinic acetylcholine receptors, which may amplify presynaptic acetylcholine release.
- Has little effect on butyrylcholinesterase, in contrast to rivastigmine, and the clinical significance of that difference is unsettled.
- The cholinergic boost improves attention, working memory and functional performance modestly without altering underlying pathology.
- Peripheral muscarinic stimulation drives nausea, vomiting, diarrhea, bradycardia and increased gastric acid secretion.

PHARMACOKINETICS

- Absorption is rapid and essentially complete with about **90%** bioavailability; food slows absorption but dosing with meals limits nausea.
- Elimination half-life is roughly **7 h**, which supports twice-daily immediate-release dosing or once-daily extended-release capsules.
- Metabolized by CYP2D6 and CYP3A4 with additional glucuronidation, and about **20%** of a dose is excreted unchanged in the urine.
- CYP2D6 poor metabolizers have around 25% higher exposure, but no dose adjustment is recommended on genotype alone.
- Both renal and hepatic impairment raise exposure meaningfully, which is why each carries a specific dose cap in the label.

ADVERSE EFFECTS

- Nausea in about **17%**, vomiting in **10%** and diarrhea in **12%** are dose-related, concentrated during titration, and often transient.
- Anorexia and weight loss are common and clinically important in frail patients, so weight is the practical tolerability measure.
- Bradycardia, syncope and atrioventricular block occur through vagotonic effects and contribute to falls and hip fracture.
- Serious skin reactions including Stevens-Johnson syndrome and acute generalized exanthematous pustulosis warrant immediate discontinuation of any rash.
- Increased gastric acid secretion raises the risk of peptic ulceration and gastrointestinal bleeding, especially with NSAIDs.
- Seizures, bladder outflow obstruction and worsening asthma or COPD are uncommon but should be anticipated in susceptible patients.

MONITORING

- Weight and appetite at every visit, since gastrointestinal intolerance and weight loss are the main reasons treatment is stopped.
- Pulse and orthostatic blood pressure at baseline and after each dose increase, with an ECG when syncope or conduction disease is present.
- Baseline and periodic renal and hepatic function, because both determine the maximum permissible dose.
- Ask about rash at every contact and stop the drug immediately if a rash appears, given the risk of severe skin reactions.
- Cognitive and functional measures every 6 months, alongside a review of total anticholinergic burden.

INTERACTIONS & CAUTIONS

- Strong CYP2D6 inhibitors such as paroxetine, fluoxetine, quinidine and bupropion raise galantamine exposure by roughly **40%**.
- Strong CYP3A4 inhibitors including ketoconazole, erythromycin and ritonavir increase exposure by about 30-40% and may require dose reduction.
- Anticholinergic drugs directly oppose the therapeutic effect and should be reviewed and stopped wherever possible.
- Additive bradycardia with beta blockers, digoxin, diltiazem, verapamil and amiodarone can produce syncope, heart block and falls.
- Succinylcholine-type neuromuscular blockade is exaggerated during anesthesia, and NSAIDs compound gastrointestinal bleeding risk.

SPECIAL POPULATIONS

- Pregnancy and lactation: there are no human data, and no plausible indication exists in patients of childbearing age.
- Pediatric safety and effectiveness have not been established and there is no approved dose for patients under 18 years.
- Geriatric patients are the intended population; the limiting factors are weight loss, bradycardia, syncope and drug burden.
- Renal impairment: cap at **16 mg/day** when creatinine clearance is 9-59 mL/min and avoid the drug entirely below 9 mL/min.
- Hepatic impairment: cap at **16 mg/day** at Child-Pugh 7-9 and do not use at Child-Pugh 10-15.

PRESCRIBING PEARLS

- Hold each step for a full **4 weeks**; nearly all the nausea comes from titrating too quickly.
- Do not use it for mild cognitive impairment: trials showed unexplained excess mortality.
- Any rash means stop; Stevens-Johnson syndrome and AGEP are labeled risks.

References

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National Institute for Health and Care Excellence. (2018). *Dementia: Assessment, management and support for people living with dementia and their carers* (NICE Guideline NG97). https://www.nice.org.uk/guidance/ng97

National Library of Medicine. (2023). Galantamine. In *MedlinePlus*. https://medlineplus.gov/druginfo/meds/a699058.html

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Stahl, S. M. (2021). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications* (5th ed.). Cambridge University Press.

NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.