CHOLINESTERASE INHIBITOR

Rivastigmine

Exelon, Exelon Patch

Dual acetyl- and butyrylcholinesterase inhibitor, the only one approved for Parkinson disease dementia and available as a transdermal patch.

USUAL ADULT DOSE	HALF-LIFE	METABOLISM	ONSET
9.5 mg/24 h patch or 6 mg PO BID	**1-2 h; enzyme block about 10 h**	**Esterase hydrolysis, not CYP**	**Benefit judged at 3-6 months**

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved for mild to moderate dementia of the Alzheimer type as capsules or patch, with the **13.3 mg/24 h** patch also approved for severe disease.
- FDA-approved for mild to moderate dementia associated with Parkinson disease, the only cholinesterase inhibitor carrying that indication.
- Widely used off-label for dementia with Lewy bodies, where the cholinergic deficit is profound and visual hallucinations may improve.
- Average benefit is modest, on the order of 2-3 points on the ADAS-cog, with the practical goal being slower functional decline.
- Not indicated for mild cognitive impairment; cholinesterase inhibitors do not prevent or delay conversion to dementia.
- The patch is generally preferred over capsules because gastrointestinal tolerability and caregiver-supported adherence are both better.

DOSING & TITRATION

- Capsules: start **1.5 mg** twice daily with food and increase by 1.5 mg twice daily at intervals of at least 2 weeks; the maximum is 6 mg twice daily.
- Patch: start **4.6 mg/24 h**, step up to the usual effective **9.5 mg/24 h** after at least 4 weeks, and to 13.3 mg/24 h in severe Alzheimer disease.
- Switching from capsules: under 6 mg daily goes to the 4.6 mg patch and 6-12 mg daily goes to the 9.5 mg patch, applied the day after the last capsule.
- If therapy is interrupted for more than **3 days**, restart at the lowest dose and re-titrate, since resuming at the old dose causes severe vomiting.
- Apply one patch only, to clean dry hairless skin on the upper back, chest or upper arm, rotating sites and avoiding the same site for 14 days.
- Consider lower maintenance doses in patients under **50 kg** and in mild to moderate renal or hepatic impairment, where exposure rises.

MECHANISM OF ACTION

- Pseudo-irreversible carbamate inhibitor of both acetylcholinesterase and butyrylcholinesterase in the central nervous system.
- Butyrylcholinesterase inhibition separates it from donepezil and galantamine and may matter more as Alzheimer disease advances.
- Raises synaptic acetylcholine in cortex and hippocampus, partially compensating for loss of basal forebrain cholinergic neurons.
- Carbamylation of the enzyme sustains inhibition for roughly **10 h** even though the drug itself clears from plasma within hours.
- Peripheral cholinergic stimulation produces the nausea, vomiting, diarrhea, bradycardia and urinary urgency that limit dosing.

PHARMACOKINETICS

- Oral bioavailability is about **36%** at 3 mg; food slows absorption and lowers peak levels, which is why capsules are taken with meals.
- Plasma half-life is only **1-2 h**, but the duration of cholinesterase inhibition is far longer at roughly 10 h after a dose.
- Cleared by cholinesterase-mediated hydrolysis to a decarbamylated metabolite with minimal CYP450 involvement, so CYP interactions are few.
- Metabolites are excreted renally and protein binding is low at about **40%**, leaving little room for displacement interactions.
- The patch produces smoother concentrations with a lower peak and comparable total exposure, which is the basis of its better tolerability.

ADVERSE EFFECTS

- Oral therapy causes nausea in up to **47%** and vomiting in about **31%**, the worst gastrointestinal profile of the cholinesterase inhibitors.
- The patch cuts nausea to roughly **7-10%** but adds application-site erythema and pruritus, occasionally true allergic contact dermatitis.
- Anorexia and clinically meaningful weight loss are common, and a documented fall in weight is a legitimate reason to stop the drug.
- Bradycardia, syncope, sinoatrial and atrioventricular block can occur and contribute to falls and hip fracture in frail patients.
- Increased gastric acid secretion raises ulcer and gastrointestinal bleeding risk, particularly alongside NSAIDs or anticoagulants.
- Seizures, worsening bronchospasm in asthma or COPD, and urinary outflow symptoms are less common but clinically important.

MONITORING

- Weight at every visit, since anorexia and weight loss are the commonest reasons treatment fails in this population.
- Pulse and orthostatic blood pressure at baseline and after each increase, with an ECG if there is syncope, bradycardia or conduction disease.
- Cognitive and functional measures such as MMSE, MoCA or an activities-of-daily-living scale every 6 months to justify continuation.
- Inspect patch application sites for spreading erythema or vesicles, which suggest contact allergy and preclude oral rechallenge.
- Review the anticholinergic burden at each visit, because coprescribed oxybutynin or diphenhydramine directly cancels the benefit.

INTERACTIONS & CAUTIONS

- Anticholinergic drugs including oxybutynin, diphenhydramine, tricyclics and paroxetine pharmacologically oppose the effect and should be deprescribed.
- Additive bradycardia occurs with beta blockers, digoxin, diltiazem, verapamil and amiodarone, and can precipitate syncope and falls.
- Exaggerated neuromuscular blockade follows succinylcholine, so anesthesia teams must be told the patient is on a cholinesterase inhibitor.
- NSAIDs combined with increased gastric acid secretion raise the risk of peptic ulceration and gastrointestinal hemorrhage.
- Because clearance is not CYP-mediated, CYP interactions are negligible, though smoking increases rivastigmine clearance by roughly a quarter.

SPECIAL POPULATIONS

- Pregnancy and lactation: no human data and no indication in this age group, so use is essentially never appropriate.
- Pediatric safety and effectiveness have not been established and there is no approved use in patients under 18 years.
- Geriatric patients are the target population; the practical limits are weight loss, bradycardia, syncope and falls rather than cognition.
- Renal or hepatic impairment raises exposure substantially, so use lower maintenance doses and titrate more slowly in mild to moderate disease.
- Body weight under **50 kg** predicts more nausea, vomiting and weight loss, and often calls for a lower target dose than the label maximum.

PRESCRIBING PEARLS

- The patch causes far less nausea than capsules; **9.5 mg/24 h** is the usual effective dose.
- Off the drug more than **3 days**? Re-titrate from the start or expect violent vomiting.
- It is the only cholinesterase inhibitor approved for Parkinson disease dementia.

References

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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.