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## DONEPEZIL (Aricept, Adlarity) Fact Sheet [G]

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### Bottom Line:

Donepezil is the cholinesterase inhibitor with the longest track record and with which we have the most experience. It is generally considered the first-line agent for dementia. Though not a cure, it delays dementia progression by six to 12 months.

### FDA Indications:

**Mild to moderate Alzheimer's dementia** (5 mg, 10 mg); **moderate to severe Alzheimer's dementia** (10 mg, 23 mg).

### Off-Label Uses:

Other memory disorders; mild cognitive impairment.

### Dosage Forms:

- **Tablets (G):** 5 mg, 10 mg, 23 mg.
- **Orally disintegrating tablets (Aricept ODT, [G]):** 5 mg, 10 mg.
- **Transdermal patch (Adlarity):** 5 mg, 10 mg.

### Dosage Guidance:

- Mild to moderate dementia: Start 5 mg QAM and ↑ to 10 mg QAM after four to six weeks.
- Moderate to severe dementia: May ↑ further to 23 mg QAM after at least three months (range 10–23 mg/day).
- Patch may be used for mild, moderate, or severe dementia: Start 5 mg Qweek and ↑ after four to six weeks to maximum 10 mg Qweek. If patient has been on 10 mg/day oral for minimum of four to six weeks, may start with 10 mg patch.

**Monitoring:** No routine monitoring recommended unless clinical picture warrants.

**Cost:** \$; Adlarity: \$\$\$\$

### Side Effects:

- Most common: Dose-related diarrhea, nausea, vomiting, weight loss (especially 23 mg/day dose), anorexia, insomnia, abnormal dreams, application site reactions (patch).
- Serious but rare: Cholinesterase inhibitors may have vagotonic effects that may cause bradycardia and/or heart block with or without a history of cardiac disease; syncope reported.

### Mechanism, Pharmacokinetics, and Drug Interactions:

- Acetylcholinesterase (AChE) inhibitor.
- Metabolized primarily through CYP2D6 and CYP3A4; t<sub>1/2</sub>: 70 hours (91 hours for patch).
- Avoid use with anticholinergic agents as they will diminish therapeutic effects; avoid beta blockers due to risk of bradycardia. CYP450 interactions not usually clinically important.

### Clinical Pearls:

- Donepezil is our first-line AChE inhibitor because of its good track record and tolerability.
- Donepezil is the second drug to be approved for dementia after tacrine, which was pulled from the market due to liver toxicity; donepezil is also the most prescribed of the three cholinesterase inhibitors. It received additional FDA approval for use in severe dementia (in addition to its initial approval for mild to moderate dementia).
- Although the manufacturer recommends bedtime dosing, we recommend starting it in the morning to minimize insomnia and vivid dreams.
- GI side effects usually resolve in one to two weeks.
- Based on a Cochrane review, donepezil causes fewer side effects than rivastigmine.

### Fun Fact:

Donepezil has been studied in children for autism, pervasive developmental disorders, ADHD, and tic disorders; however, the minimal data do not support such use.