

Appendix 5: Cholinesterase inhibitors for treatment of mild-to-moderate dementia

| | Donepezil (Aricept®) | Rivastigmine (Exelon®) | Galantamine (Reminyl®)* |
|--|---|--|---|
| Dosing | | Take with food | Take with food |
| Initial dose | 5 mg qAM | 1.5 mg bid | 8 mg od |
| Minimal effective dose | 5 mg qAM | 3 mg bid | 16 mg od |
| Usual dose | 10 mg qAM | 4.5-6 mg bid | 16-24 mg od |
| Dose titration | 4-week intervals | 4-week intervals | 4-week intervals |
| Selectivity | Acetyl cholinesterase inhibitor | Acetyl cholinesterase inhibitor and Butyryl cholinesterase inhibitor | Acetyl cholinesterase inhibitor |
| Mechanism of Action These agents inhibit acetylcholine breakdown by blocking acetylcholinesterase, increasing acetylcholine levels in the synaptic cleft and compensating for the deficit seen in Alzheimer disease. | Reversible inhibition of acetyl cholinesterase binding | Pseudo-irreversible competitive inhibition of acetyl cholinesterase and butyryl cholinesterase | Inhibits acetyl cholinesterase Nicotinic receptor modulation (may increase acetyl cholinesterase release) |
| Half-Life | 70-80 hours | 1.5 - 2 hours | 6-10 hours |
| Metabolism | CYP 2D6 and CY3A4 | Non-CYP metabolism. | CYP 2D6 and CY3A4 |
| Elimination | Liver | Kidney | Liver and Kidney |
| Drug Interaction Potential | Low; dual pathways and lack of inhibition of CYP enzymes. Caution with use with other CYP 2D6 drugs, such as some beta blockers | Very low | Low; dual pathways and lack of inhibition of CYP enzymes. Caution with use with other CYP 2D6 drugs, such as some beta-blockers. |
| Common side effects | The most common side effects are gastrointestinal and sleep disturbances. If the patient develops gastrointestinal side effects, it is recommended that the medication dose be decreased, titrated more slowly, and given with food. Cholinesterase inhibitors are contraindicated in patients with sick sinus syndrome, undiagnosed syncope, and conduction block. Caution should be used in patients with poorly controlled cholinergically mediated conditions, such as cardiac disease, peptic ulcer disease, asthma, and chronic obstructive pulmonary disease. It is appropriate to perform an electrocardiogram in patients with cardiac risk factors prior to initiating therapy with a cholinesterase inhibitor. | | |

*Extended-release tablet once daily

Sources: Drugs for Alzheimer's Disease. Therapeutics Letter. 2007. [cited 2007 Apr 4]; 56 Available from www.ti.ubc.ca
Hogan DB. The latest in drug therapy for dementia: Gleanings from the Third Canadian Conference on Diagnosis and Treatment of Dementia. *Geriatrics & Aging* 2007; 10(3):145-151.



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