Pharmacologic Agents for Dementia

Medication	Dosing & Administration	2023 Formulary Status		2024 Formulary Status		Adverse Drug Reactions
		Tier	UM	Tier	UM	
Cholinesterase Inhibitors						
donepezil tabs 5mg & 10mg, donepezil odt	5mg to 10mg PO once daily	2		2		nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue, and anorexia
galantamine er	8mg to 24mg PO once daily	2		2		dizziness, headache, decreased appetite, and weight decreased
galantamine oral soln	4mg to 12mg PO twice daily	4		4		nausea, vomiting, diarrhea
galantamine tabs	4mg to 12mg PO twice daily	2		2		nausea, vomiting, diarrhea
rivastigmine caps	1.5mg to 6mg PO twice daily	3		3		nausea, vomiting, anorexia, dyspepsia, and asthenia
rivastigmine patches	4.6mg/24 hours to 13.3mg/24 hours patch transdermally once daily	4		4		nausea, vomiting, and diarrhea
N-methyl-D-aspartate (NMDA) Receptor Antagonists						
memantine hcl immediate release	5mg to 20mg PO daily in 2 divided doses	2		2		headache, diarrhea and dizziness, vomiting
memantine hcl titration pack 5mg-10mg	5mg to 20mg PO daily in 2 divided doses	2		2		

Brand-name drugs are capitalized and generic drugs are listed in the lower-case italics.

a: Cholinesterase inhibitors. FDA labeling for AD is as follows: donepezil—mild, moderate, severe; galantamine—mild, moderate; rivastigmine—mild, moderate. Continue if patient improves or stabilizes; stopping medication can lead to rapid decline. Adverse events increase with higher dosage.
b: Approved by FDA for moderate to severe AD. Possible adverse events include dizziness, headache, somnolence. NMDA = N-methyl-d-aspartate.
c: Increased mortality found in controlled studies of mild cognitive impairment

D. Osterweil & L. Vu 09/2014; D. Osterweil & A. Phan 09/2015; D. Yoon 08/2016; L. Vuong 08/2017; D. Yoon 09/2018; K. Truong 08/2019, 08/2020; S. Cho 09/2021; K. Truong 09/2022; S. Cho 09/2023

TREATMENT OF AGITATION

- Consider non-pharmacologic approaches first before pharmacologic tx
- Consider steps to reduce non-verbalized pain
- Cognitive enhancers may slow deterioration, and agitation may worsen if discontinued. Low doses of antipsychotic medications have limited role but may be necessary. Note this use is off-label and increases risk of death compared with placebo in patients with AD. CATIE-AD trial (NEJM2006;355:1525-1538) showed modest tx benefit compared with placebo for olanzapine and risperidone that was mitigated by greater EPS, sedation, and confusion. In this trial, quetiapine did not appear to be efficacious compared with placebo but caused greater sedation.
- CATIE-AD reported second-generation antipsychotics cause weight gain, particularly in women treated with olanzapine or quetiapine; olanzapine tx was also associated with decreased HDL cholesterol
- Cholinesterase inhibitors may worsen behavioral variant in those with Frontotemporal Dementia (FTD): consider Memantine or SSRI's. For the treatment of apathy: assess and treat underlying depression; cholinesterase inhibitors help; methylphenidate (5-20 mg/d), very limited data, may cause agitation and psychosis.

Symptom	Medication	Dosing & Administration	2023 Formulary Status		2024 Formulary Status	
			Tier	UM	Tier	UM
Agitation in context of psychosis	*aripiprazole tabs*	2.5mg to 12.5mg PO daily[a]	3		3	
	olanzapine oral	2.5 to 10mg PO daily[a]	2		2	
	quetiapine ir	12.5mg to 100mg PO daily[a]	2		2	
	risperidone	0.25mg to 3 mg daily[a]	2		2	
Agitation in context of depression	SSRI	Varies	Refer to Comprehensive formulary			
	e.g., *citalopram tabs*	10 to 20mg daily	1		1	
Anxiety, mild to moderate irritability	*buspirone*	15 to 60 mg PO daily[b]	2		2	
	trazodone	50 to 100mg PO daily[c]	1		1	
Agitation or agression unresponsive to first line treatment	*carbamazepine ir*	300 to 600 mg PO daily[d]	2		2	
	divalproex sodium ir	500-1500 mg PO daily[e]	2		2	
	olanzapine inj	2.5 to 5 mg IM [a,f]	2		2	
Sexual aggression, impulse-control symptoms in men	Second-generation antipsychotic or divalproex	see dosages above	see above			

a: Avoid: Greater mortality, cardiovascular, and cerebrovascular events than placebo; use with particular caution in patients with cerebrovascular disease, prolonged QTc interval or hypovolemia.
b: Can be given Q12h; allow 2-4 wk for adequate trial.
c: Small divided daytime dosage and larger bedtime dosage; watch for sedation and orthostasis.
d: Monitor serum levels; periodic CBCs, platelet counts secondary to agranulocytosis risk. Beware of drug-drug interactions.
e: Can monitor serum levels; usually well tolerated; check complete blood count (CBC), platelets for agranulocytosis, thrombocytopenia risk.
f: For acute use only; initial dose 2.5 mg to 5 mg, second dose (2.5 mg to 5 mg) can be given after 2 hr, maximum of 3 injections in 24 hr (maximum daily dose 20mg); should not be administered for more than 3 consecutive days.

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