

DRUGS FOR ALZHEIMER'S DISEASE

From Lippincott

By Fatima Haider

Dementia of the Alzheimer type has three distinguishing features:

- 1) accumulation of senile plaques (β -amyloid accumulations)
- 2) formation of numerous neurofibrillary tangles
- 3) loss of cortical neurons, particularly cholinergic neurons.

Current therapies aim to either improve cholinergic transmission within the CNS or prevent excitotoxic actions resulting from overstimulation of NMDA-glutamate receptors in selected areas of the brain.

	ACETYLCHOLINESTERASE INHIBITORS	NMDA RECEPTOR ANTAGONIST
DRUG NAMES	Donepezil Galantamine Rivastigmine	Memantine
MOA	reversible AChE inhibitor	Binding of glutamate to the NMDA receptor assists in the opening of an ion channel that allows Ca^{2+} to enter the neuron. (Excess intracellular Ca^{2+} can activate a number of processes that ultimately damage neurons and lead to apoptosis.)
THERAPEUTIC USES	-At best, these compounds provide a modest reduction in the rate of loss of cognitive functioning in Alzheimer patients. -Rivastigmine is the only agent approved for the management of dementia associated with Parkinson's disease and also the only AChE inhibitor available as a transdermal formulation.	-Memantine indicated for moderate to severe Alzheimer's disease.

ADVERSE EFFECTS	nausea, diarrhea, vomiting, anorexia, tremors, bradycardia, and muscle cramps	Memantine is well tolerated, with few dose-dependent adverse events. Expected side effects, such as confusion, agitation, and restlessness, are indistinguishable from the symptoms of Alzheimer's disease.
------------------------	---	---

DRUGS USED IN MULTIPLE SCLEROSIS

Multiple sclerosis is an autoimmune inflammatory demyelinating disease of the CNS.

Drugs currently approved for MS are indicated to decrease relapse rates or in some cases to prevent accumulation of disability. The major target of these medications is to modify the immune response through inhibition of white blood cell-mediated inflammatory processes that eventually lead to myelin sheath damage and decreased or inappropriate axonal communication between cells.

	THERAPEUTIC USES	ADVERSE EFFECTS
Interferon β1a and interferon β1b	The immunomodulatory effects of interferon help to diminish the inflammatory responses that lead to demyelination of the axon sheaths.	depression, local injection site reactions, hepatic enzyme increases, and flulike symptoms.
Glatiramer	a synthetic polypeptide that resembles myelin protein and may act as a decoy to T-cell attack	Some patients experience a postinjection reaction that includes flushing, chest pain, anxiety, and itching. It is usually self-limiting
Fingolimod	an oral drug that alters lymphocyte migration, resulting in fewer lymphocytes in the CNS.	-may cause first-dose bradycardia -is associated with an increased risk of infection and macular edema
Teriflunomide	an oral pyrimidine synthesis inhibitor that leads to a lower concentration of active lymphocytes in the CNS.	-may cause elevated liver enzymes. -It should be avoided in pregnancy.
Dimethyl fumarate	an oral agent that may alter the cellular response to oxidative stress to reduce disease progression.	Flushing and abdominal pain
Natalizumab	a monoclonal antibody indicated for MS in patients who have failed first-line therapies	
Mitoxantrone	a cytotoxic anthracycline analog that kills T cells and may also be used for MS.	

SYMPTOMATIC TREATMENT: Many different classes of drugs are used to manage symptoms of MS such as spasticity, constipation, bladder dysfunction, and depression. **Dalfampridine**, an oral potassium channel blocker, improves walking speeds in patients with MS. It is the first drug approved for this use.

DRUGS USED IN AMYOTROPHIC LATERAL SCLEROSIS

ALS is characterized by progressive degeneration of motor neurons, resulting in the inability to initiate or control muscle movement.

Riluzole, an NMDA receptor antagonist, is currently the only drug indicated for the management of ALS. It is believed to act by inhibiting glutamate release and blocking sodium channels.

Riluzole may improve survival time and delay the need for ventilator support in patients suffering from ALS.