Alzheimer’s disease is the most common neurodegenerative disorder and a highly prevalent cause of dementia with aging. Several pathophysiological events are triggered in Alzheimer’s disease that ultimately lead to signaling pathway dysfunction, failure of neurotransmission, and neuronal death. **Memantine (M1749)** is used as a treatment to slow the progression of this disease.

Several neuroprotective compounds inhibit cholinergic signaling to improve cognitive abilities. Memantine instead acts as a noncompetitive antagonist at NMDA receptors, blocking glutamate signaling. Memantine inhibits prolonged influx of calcium ions from extrasynaptic receptors, lessening neuronal excitotoxicity.

Memantine also interacts with a variety of ligand-gated ion channels such as nicotinic acetylcholine receptors (nAChRs), dopamine receptors, and serotonin receptors. Most of this activity does not contribute to the effects of memantine on cognitive function, although it may be related to the antidepressant, antitussive, and antinociceptive activities of memantine.

At therapeutic concentrations, memantine promotes synaptic plasticity and preserves or enhances memory in animal models of Alzheimer’s disease. Additionally, memantine protects against excitotoxic neurodegeneration. Additional research indicates that memantine suppresses toxicity induced by amyloid-β (Aβ) plaque formation, potentially inhibiting the production of Aβ by altering APP processing.

References: