CNS Drug Reviews
Vol. 8, No.2, pp. 159–176

Galantamine — a Novel Cholinergic Drug with a Unique Dual Mode of Action for the Treatment of Patients with Alzheimer's Disease

Sean Lilienfeld

Janssen Research Foundation, Titusville, New Jersey, 08560, USA

Key Words: Galantamine—Acetylcholinesterase inhibitor—Alzheimer's disease—Nicotinic modulator.

ABSTRACT

Galantamine hydrobromide is a tertiary alkaloid drug that has been developed and approved in a number of countries including the USA and several countries in Europe as a treatment for mild-to-moderate Alzheimer's disease (AD). Galantamine has a unique, dual mode of action. It is a reversible, competitive inhibitor of acetylcholinesterase (AChE), and is the only drug actively marketed for the treatment of AD with proven activity as an allosteric modulator of nicotinic acetylcholine receptors (nAChRs). This latter activity is thought to be particularly important since decreases in the expression and activity of nAChRs make a large contribution to the reduction in central cholinergic neurotransmission in patients with AD. Galantamine exhibits favorable pharmacokinetic characteristics including predictable linear elimination kinetics at the recommended maintenance doses (16 and 24 mg/day), a relatively short half-life (approximately 7 h) and high bioavailability. It is extensively metabolized in numerous pathways, mainly in the liver via cytochrome P450 enzymes CYP2D6 and CYP3A4, and has a low potential for clinically significant drug–drug interactions. During four large randomized, double-blind, placebo-controlled trials of up to 6 months duration, galantamine 16 and 24 mg/day significantly benefited cognitive and global function, ability to perform activities of daily living (ADL) and behavior, relative to placebo and baseline, for up to 6 months. Caregiver burden (time spent by caregivers supervising patients or assisting them with ADL), and caregiver distress (related to patients' behavioral symptoms) were also reduced. Cognitive and functional abilities were preserved at or near baseline for at least 12 months in patients who received galantamine 24 mg/day for 12 months in a long-term US study. These benefits were maximized by early and continued galantamine treatment and, again, were associated with significant reductions in caregiver burden. Trials of the efficacy of galantamine in dementia related to cerebrovascular disease have also yielded positive results.

There are no safety concerns associated with the use of galantamine. The incidence of adverse events, particularly cholinergically mediated events affecting the gastrointestinal system, is generally low and can be minimized using the recommended slow dose-escalation scheme. Galantamine may, therefore, help to reduce the overall burden and cost involved in caring for dementia patients. Taking all evidence into account, galantamine has the potential to become a first-line therapy for dementia.