In people with moderate-to-severe dementia in Alzheimer's disease (AD), memantine provides some clinical benefits. It is commonly administered twice daily at a maximum dose of 20 mg. To improve medication adherence, convenience of use and to enable a higher daily dose, a 28 mg, extended-release formulation of memantine has been developed. We review the results of a Phase III randomized and controlled trial of memantine extended release as an add-on treatment and compared the findings with a similarly designed previous trial evaluating the immediate release (IR) form. Memantine extended release produced minor benefits on cognitive ability, including verbal fluency, behavioral problems and global clinical assessment. There was no difference between the treatment groups on activities of daily living. The observed effects were not larger than those of the IR formulation tested in a similar setting. The lack of impact on activities of daily living suggests that the small improvements in cognition and behavior did not translate into clinically important changes. In conclusion, there is no convincing evidence that the novel once-daily formulation of memantine represents a significant progress in the clinical management of AD that would justify additional treatment costs.