NEMDAA (Memantine)

Available as tablets: 5 mg, 10 mg

(1) Indications (for elderly): Treatment of patients with moderate to severe Alzheimer's disease.

(2) Recent trials:

Abstract 1:

Analysis of the effect of memantine in reducing the worsening of clinical symptoms in patients with moderate to severe Alzheimer's disease.

Wilkinson D, Andersen HF.
Dement Geriatr Cogn Disord. 2007;24(2):138-45. Epub 2007 Jul 4.

BACKGROUND: Alzheimer's disease (AD) is a progressive neurodegenerative disorder and delaying disease worsening is a relevant treatment outcome.

METHODS: Data from 6 randomized, double-blind, placebo-controlled, 6-month studies were pooled and a subgroup of patients (867 on placebo, 959 on memantine) with moderate to severe AD (Mini- Mental State Examination <20) was analyzed. 'Any clinical worsening' was defined as a decline on the Alzheimer's Disease Assessment Scale - Cognitive Subscale (ADAS-cog) or the Severe Impairment Battery (SIB) and on the Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-plus) and the Alzheimer's Disease Cooperative Study - Activities of Daily Living Inventory (ADCS-ADL), and 'marked clinical worsening' as > or = 4 points decline on the ADAS-cog or > or = 5 points on the SIB and decline on the CIBIC-plus and the ADCS-ADL.

RESULTS: More placebo-treated than memantine-treated patients showed any clinical worsening (28 vs. 18%; $p < 0.001$), and 21% placebo-treated patients compared to 11% memantine-treated patients had marked clinical worsening ($p < 0.001$).

CONCLUSION**: In this population of moderate and severe AD patients, treatment with memantine was associated with reducing worsening of clinical symptoms in AD during the 6-month study period.**

Abstract 2:

Memantine for agitation/aggression and psychosis in moderately severe to severe Alzheimer's disease: a pooled analysis of 3 studies.

Wilcock GK, Ballard CG, Cooper JA, Loft H.

J Clin Psychiatry. 2008 Mar;69(3):341-8.

OBJECTIVE: Long-standing evidence indicates that Alzheimer's disease patients with behavioral symptoms have a worse prognosis and a more rapid disease progression. The current retrospective analysis evaluated the efficacy and safety of memantine in a subpopulation of patients with Alzheimer's disease exhibiting behavioral symptoms of agitation/aggression or psychosis at baseline.

METHOD: A pooled analysis was conducted in people with agitation/aggression or psychosis from 3 large 6-month, randomized studies in moderately severe to severe Alzheimer's disease. The effect of memantine and placebo on these specific symptoms was evaluated using the Neuropsychiatric Inventory (NPI) subitem cluster of agitation and psychosis. Outcomes on global, cognitive, and functional measures were also analyzed.

RESULTS: Sixty percent of the total patient group had baseline symptoms of agitation/aggression, delusions, or hallucinations on the NPI. At both 12 and 24/28 weeks, there was a significant treatment advantage for memantine over placebo for the proportion of patients showing improvement on the defined neuropsychiatric symptom cluster (55.6% vs. 44.4% at week 12, $p = .008$; 58.0% vs. 44.8% at week 24/28, $p = .002$) and specifically for the treatment of agitation/aggression (55.3% vs. 43.1% at week 12, $p = .011$; 61.0% vs. 45.0% at week 24/28, $p < .001$). Placebo-treated patients in this population demonstrated an accelerated disease progression for global (Clinician's Interview-Based Impression of Change Plus Caregiver Input), cognitive (Severe Impairment Battery), and functional (Alzheimer Disease Cooperative Study Activities of Daily Living Inventory 19-item scale) outcomes, but memantine conferred statistically significant benefit for all measures. Tolerability in this population remained good, and fewer memantine-treated patients than placebo-treated patients withdrew due to adverse events.

CONCLUSIONS: **This post hoc analysis provides important evidence from placebo-controlled trials that memantine may be a safe and effective treatment in Alzheimer's disease patients with agitation/aggression or psychosis, who are otherwise prone to rapid progression. Memantine treatment provided benefits in cognitive, functional, and global outcomes in these patients and for their agitation/aggression.**

Abstract 3:

Pooled analyses on cognitive effects of memantine in patients with moderate to severe Alzheimer's disease.

Emre M, Mecocci P, Stender K.
J Alzheimers Dis. 2008 Jun;14(2):193-9.

Alzheimer's disease (AD) is a progressive neurodegenerative disorder, constituting the most common cause of dementia. Memantine, an N-methyl-D-aspartate receptor antagonist indicated for the treatment of moderate to severe AD, has been shown to provide benefits in cognitive, functional, and behavioral domains in large, randomized clinical trials. The current analysis combined data from six previously published studies and assessed the effect of memantine on various cognitive functions in 1826 patients (867 on placebo and 959 on memantine) with moderate to severe AD (MMSE<20). The Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog) and the Severe Impairment Battery (SIB) scores from all six studies were pooled and combined into three clusters representing discrete cognitive domains: language, memory, and praxis. At baseline, there were no clinically significant differences between the memantine- and placebo-treated groups. **After 24 weeks, responder analyses revealed that memantine treatment resulted in statistically significantly more patients improving on each of the three clusters, language, memory, and praxis, compared with placebo, and a lower percentage of patients treated with memantine showed any worsening on any of the three clusters compared with patients receiving placebo. It is concluded that treatment with memantine provides benefits in all three cognitive functions.**

(3) Dosage in elderly:

On the basis of the clinical studies, the recommended dose for patients over the age of 65 years is 20 mg per day (10 mg twice a day).

In order to reduce the risk of side effects the maintenance dose is achieved by upward titration of 5 mg per week over the first 3 weeks as follows:

Treatment should be started with 5 mg daily (5 mg tab. in the morning) during the 1st week. In the 2nd week 10 mg per day (5 mg tab. twice a day) and in the 3rd week 15 mg per day (10 mg morning and 5 mg evening) is recommended. From the 4th week on, treatment can be continued with the recommended maintenance dose of 20 mg per day (10 mg twice a day).

The tablets can be taken with or without food.

(4) Common side effects:

In general, observed side effects are mild to moderate. The most common side effects are headache, somnolence, constipation and dizziness. Less frequently tiredness, confusion, vomiting, abnormal gait and hallucinations (mainly seen in patients with severe Alzheimer’s disease) have been reported.