



**So that memories
don't fade away**

In Alzheimer's disease,

Recommend,

LARENTINE

Memantine Hydrochloride 5 mg and 10 mg Tablets

LARENTINE-D

Memantine Hydrochloride with
Donepezil Hydrochloride Tablets / 5 mg & 5 mg, 10 mg & 5 mg

Background:

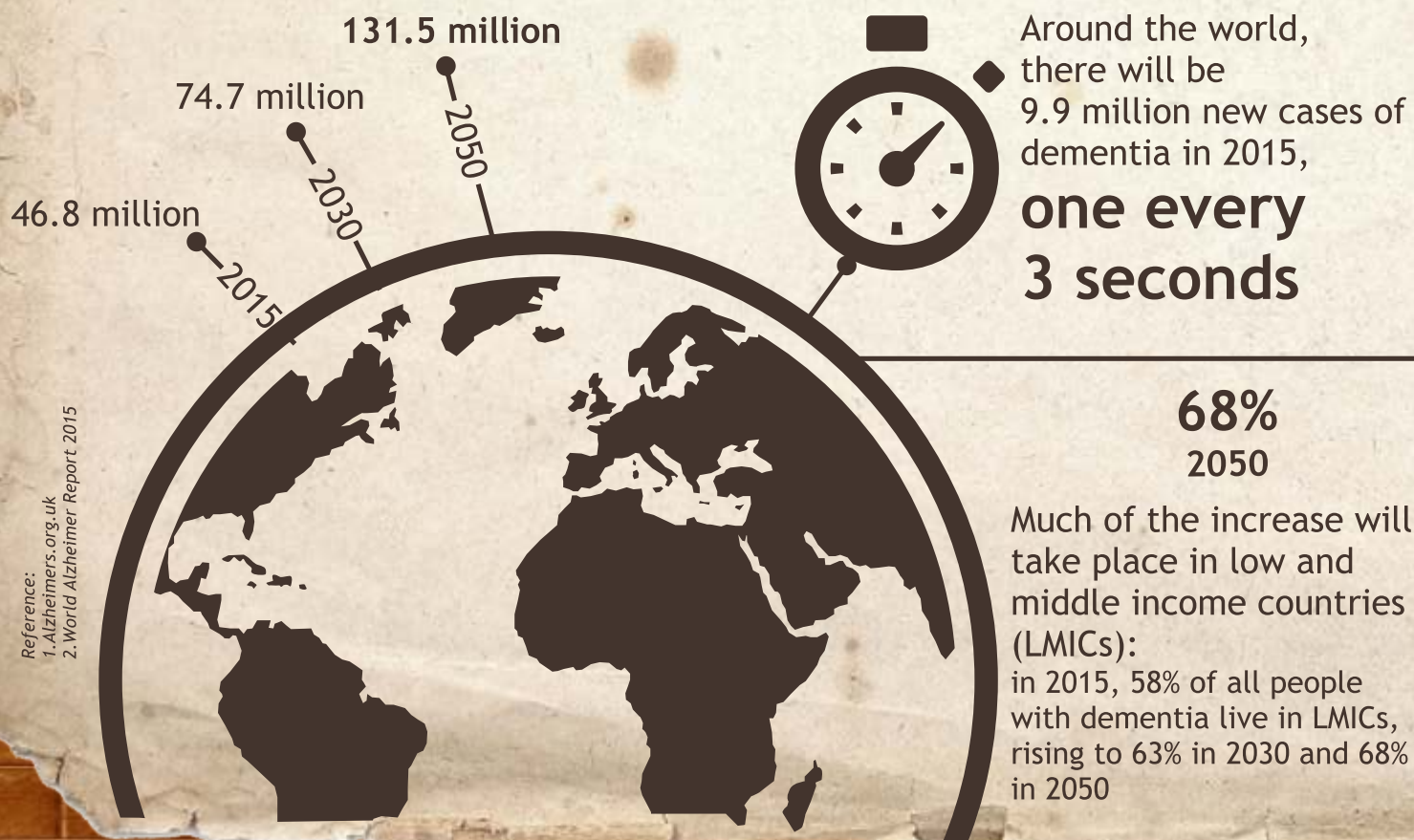
Alzheimer's is a neurodegenerative disease, named after the doctor who first described it (Alois Alzheimer), is a physical disease that affects the brain. Alzheimer's disease is the most common cause of dementia. The word dementia describes a set of symptoms that can include memory loss and difficulties with thinking, problem-solving or language. These symptoms occur when the brain is damaged by certain diseases, including Alzheimer's disease.¹

The global impact of dementia

- About 46.78 million people worldwide are living with dementia in 2015 & this number will almost double every 20 years (74.7 million in 2030 and 131.45 million in 2050)²
- Around the world, there will be 9.9 million new cases of dementia in 2015, i.e. one every 3 seconds.²
- Much of the increase will take place in low and middle income countries (LMICs): in 2015, 58% of all people with dementia live in LMICs, rising to 63% in 2030 and 68% in 2050.²
- In 2010, 3.7 million Indians were suffering with dementia.²

46.8 million people worldwide are living with dementia in 2015.

This number will almost double every 20 years.

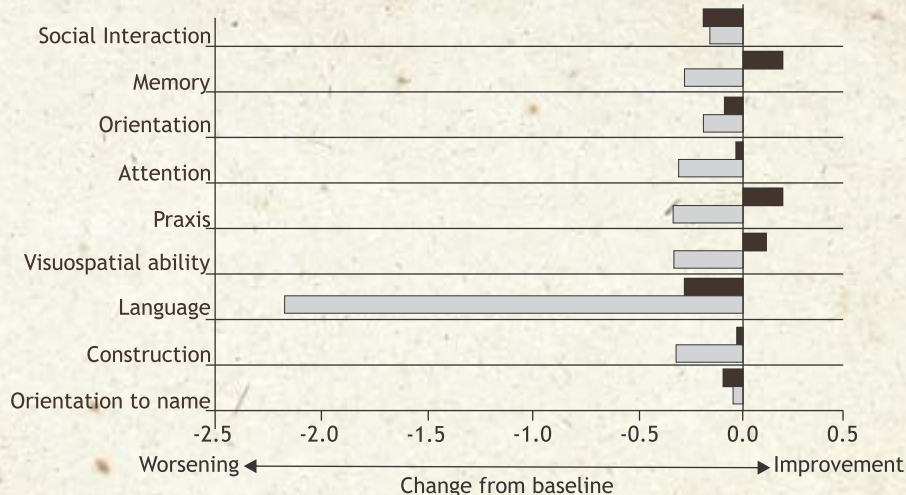


Clinical Effectiveness:

Memantine is an N-methyl-D-aspartate receptor antagonist used to treat AD in more than 80 countries worldwide.

Study on 633 patients for 24 weeks; in comparison to placebo

- Memantine provide better cognition, attention, praxis, visuospatial ability and language,
- Improves behavioral and psychological symptoms, including activity disturbances and aggressiveness



Source: Expert Opin. Pharmacother. (2014) 15(7)

Fig: Summary statistics of domain-specific changes in Severe Impairment Battery-Japanese version scores from baseline to week 24 (full analysis set, last observation carried forward analysis). The difference between the FAS (633 patients; memantine, n = 618; placebo, n = 615) and LOCF (631 patients) is due to a lack of baseline data in two patients. FAS: Full analysis set; LOCF: Last observation carried forward.

As per “Alzheimer's Research & Therapy Journal; 2015”

- Study on 1408, individuals with moderate to severe AD for six months suggests that:
- Addition of memantine to stable donepezil provides at least 50% greater clinical benefits than the individual those of monotherapies.

AUC improvements relative to placebo

| Evaluation | PBO number = 281 | MEM number = 289 | PBO-DON number = 418 | MEM-DON number = 429 |
|--------------------------|---------------------|---------------------|-------------------------|-------------------------|
| SIB AUC0-24 | -51.4 ± 10.9 | 4.9 ± 10.5 | 27.5 ± 8.6 | 67.4 ± 8.3 |
| ADCS-ADL19 { AUC0-24} | -32.7 ± 6.4 | -12.2 ± 6.2 | -9.5 ± 5.0 | 1.4 ± 4.9 |
| NPId (AUC0-24) | 22.4 ± 12.2 | -7.3 ± 11.8 | -27.2 ± 9.7 | -74.3 ± 9.4 |
| CIBIC-Plus (AUC0-24) | 6.0 ± 1.1 | 2.0 ± 1.0 | 1.4 ± 0.9 | -2.1 ± 0.8 |
| 4D-CI { AUC0-24} | -175.4 ± 63.7 | 152.1 ± 61.5 | 344.7 ± 50.4 | 630.0 ± 49.0 |

aMean ± SE (point x week); dfor NPI, lower score indicates improvement. 4D-CI, four-dimensional composite index; ADCS-ADL19, 19-item Alzheimer's Disease Cooperative Study Activities of Daily Living scale; AUC, area under the curve; CIBIC-Plus, Clinician's Interview-Based Impression of Change - Plus Caregiver Input; MEM, memantine; MEM-DON, memantine added to background donepezil treatment; NPI, Neuropsychiatric Inventory; PBO, placebo; PBO-DON, placebo added to background donepezil treatment; SE, standard error of the mean; SIB, Severe Impairment Battery

The AUC method has the potential to 'smooth the data' of patients whose visit-by-visit scores are prone to variations, thereby potentially increasing the signal-to-noise ratio.

LARENTINE

Memantine Hydrochloride 5 mg and 10 mg Tablets

LARENTINE-D

Memantine Hydrochloride with
Donepezil Hydrochloride Tablets 5 mg & 5 mg, 10 & 5 mg

Description:

LARENTINE is a film coated tablet containing memantine which is prescribed to improve memory, attention, reason, language and the ability to perform simple tasks. It can be used alone or with other Alzheimer's disease treatments.

LARENTINE-D is a film coated tablet containing combination of memantine with donepezil. Continued treatment with donepezil is associated with cognitive benefits.

Mechanism of Action:

Memantine exerts its action through uncompetitive NMDA receptor antagonism, binding preferentially to the NMDA receptor-operated cation channels. Prolonged increased levels of glutamate in the brain of demented patients are sufficient to counter the voltage-dependent block of NMDA receptors by Mg^{2+} ions and allow continuous influx of Ca^{2+} ions into cells, ultimately resulting in neuronal degeneration. Studies suggest that memantine binds more effectively than Mg^{2+} ions at the NMDA receptor, and thereby effectively blocks this prolonged influx of Ca^{2+} ions through the NMDA channel whilst preserving the transient physiological activation of the channels by higher concentrations of synaptically released glutamate. Thus memantine protects against chronically elevated concentrations of glutamate. Memantine also has antagonistic activity at the type 3 serotonergic (5-HT₃) receptor with a potency that is similar to that at the NMDA receptor, and lower antagonistic activity at the nicotinic acetylcholine receptor. This drug has no affinity for γ -aminobutyric acid (GABA), benzodiazepine, dopamine, adrenergic, histamine, or glycine receptors or for voltage-dependent calcium, sodium, or potassium channels.

Donepezil is a piperidine derivative that is a centrally active, reversible inhibitor of acetylcholinesterase. This drug is structurally unrelated to other anticholinesterase agents. Donepezil's proposed mechanism of action involves the reversible inhibition of cholinesterases (eg. acetylcholinesterase), which prevents the hydrolysis of acetylcholine, and leads to an increased concentration of acetylcholine at cholinergic synapses. Evidence suggests that the anticholinesterase activity of donepezil is relatively specific for acetylcholinesterase in the brain. It works by increasing the amount of acetylcholine in the brain, which helps in improving mental function.

Dosage:

Take Memantine exactly as directed by your doctor. Do not take more or less than instructed by your doctor.

Initial dose: 5 mg orally once a day, then titrated upwards by 5 mg per week

Maintenance dose: 5 mg once a day up to 10 mg twice a day

Maximum dose: 20 mg per day

Administration: -

Administered orally by mouth, as directed by doctor

Presentation: Available as strip of 10 tablets.

Storage:

Store at a temperature between 20° C to 25° C

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