Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Levetiracetam

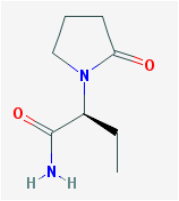
Evidence Summary

Cognitive benefits with levetiracetam have been observed in people with epilepsy, MCI, and in healthy elderly; it has some side effects including drowsiness, fatigue, irritability, and increased infections.

Neuroprotective Benefit: Cognitive benefits have been observed in healthy elderly, MCI patients, epilepsy patients, and Alzheimer's patients with epilepsy. Several clinical trials in Alzheimer's patients are ongoing.

Aging and related health concerns: Although a few case studies suggested relief from peripheral neuropathy, a meta-analysis failed to find significant effects.

Safety: Numerous clinical trials have found that levetiracetam is well-tolerated but is associated with somnolence, fatigue, dizziness, irritability, and nasopharyngitis/infections. There are major drug interactions with pain killers and caffeine.

Availability: prescription	**Dose**: 1,000-4,000 mg/day in epilepsy patients; 500-1,000 mg/day in a currently ongoing clinical trial in AD patients	**Chemical formula:** $C_8H_{14}N_2O_2$ **MW**: 170.212  Source: PubChem
Half life: 6-8 hours	**BBB**: penetrant	
Clinical trials: the largest meta-analysis included 26 RCTs with 2,832 patients	**Observational studies**: most have been in epilepsy patients. One longitudinal study included 109 subjects, 40 on LEV.	

What is it? Levetiracetam (brand name Keppra) is an atypical anti-epileptic prescription medication approved in 1999 as a second-generation drug. It is most often used as an add-on therapy in the treatment of epilepsy. The precise mechanism through which levetiracetam exerts its effects is unknown. Functionally, it selectively prevents hypersynchronization of epileptiform burst firing and propagation of seizure activity (DrugBank). Molecularly, levetiracetam has high affinity for the presynaptic membrane protein SV2A, which is widely expressed throughout the brain including high levels in the hippocampus [1]. Levetiracetam acts as an agonist at SV2A, which in turn inhibits neurotransmitter release (DrugBank). Based on the strong linear correlation between affinity to SV2A and the ability to protect against seizures in a mouse model of audiogenic seizure, it appears that action on SV2A is one of levetiracetam's main mechanisms of action, though other targets have also been proposed (discussed below).

Neuroprotective Benefit: Cognitive benefits have been observed in healthy elderly, MCI patients, epilepsy patients, and Alzheimer's patients with epilepsy. Several clinical trials in Alzheimer's patients are ongoing.

Types of evidence:

- 2 meta-analyses in patients with seizures/epilepsy
- 8 controlled clinical trials in various patient populations
- 4 open-label trials
- 1 case study in Lewy Body Dementia
- 3 fMRI studies

- 1 observational study in glioma patients
- Numerous laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function?

Numerous studies have been carried out in humans, though most have been in patients with epilepsy/seizures.

Epilepsy patients: BENEFIT. In a 2012 Cochrane meta-analysis of 11 randomized controlled trials (total of 1,861 subjects) in drug-resistant focal epilepsy patients, add-on levetiracetam treatment (1,000-4,000 mg/day in adults, 60 mg/kg/day in children) for 12 -24 weeks significantly reduced focal seizure frequency and had a positive effect on cognition and some aspects of quality of life in adults [2]. However, in children, levetiracetam did not appear to alter cognitive functions.

In an open-label trial of 55 drug-naïve epilepsy patients, levetiracetam monotherapy for 1 year significantly improved verbal and visual attention, psychomotor speed, mental flexibility, executive function, verbal fluency and word generation [3]. There were 25 measures of cognitive functions plus 2 measures of mood, of which 14 cognitive measures had p-values under 0.05 (difference between pre-treatment and post-treatment). None of the neuropsychological domains showed significant decline. No changes in mood were found.

A smaller open-label trial of 27 patients with drug-resistant epilepsy also reported that levetiracetam add-on treatment (500 mg/day initially, then increased up to 1,000-3,000 mg/day) for 1 year significantly improved measurements of prospective memory, working memory, motor functions, verbal fluency, attention, and quality of life [4]. As in the study above, the study was small and there was no control group.

Healthy adults: UNKNOWN. In a small placebo-controlled clinical study of 12 healthy adults, a single dose of levetiracetam (500 mg) significantly improved visual attention as measured by the Trail Making Test Part A [5]. No differences were seen in other neuropsychological parameters such as working memory, inhibitory control of attention, planning, and decision-making. It is difficult to extrapolate these findings to potential benefits with chronic treatment.

Healthy elderly: POTENTIAL/MIXED BENEFIT. In a double-blind randomized controlled cross-over trial in 20 healthy elderly (65-80 years old), 6 weeks of levetiracetam treatment (250 mg twice daily for 2

weeks, then increased to 500 mg twice daily, then tapered back to 250 mg twice daily) significantly improved visual memory (MCG Complex Figure Recall) and 2 attention tests (Trail Making Test Part A and Stroop Interference) compared to placebo [6]. However, there were 29 other tests that failed to show a difference compared to placebo, so it is unclear whether the significant improvements occurred by chance. There was a trend for greater irritability and fatigue during the levetiracetam phase. Effect-size changes were generally small (Cohen d < 0.5) and no effects were seen for psychomotor speed or language.

Amnestic MCI patients: BENEFIT. People with amnestic mild cognitive impairment (aMCI) have hyperactivity in the hippocampus (dentate gyrus/CA3 region) during episodic memory tasks [7]. In a functional MRI study that included 54 aMCI patients, this hyperactivity was significantly greater compared to an aged control group without aMCI (n=17). When aMCI patients were treated with 62.5 or 125 mg twice daily doses of levetiracetam, there was a significant improvement in memory task performance including improved accuracy and reduced errors, while normalizing fMRI activation in the hippocampus. Higher dosing at 250 mg twice daily had no significant benefit on fMRI activation and less pronounced cognitive benefits, suggesting that there is an optimal dose for optimal performance.

In an older study from the same group, a randomized controlled trial in 17 aMCI reported that levetiracetam treatment (125 mg twice daily) for 2 weeks reduced hippocampal activation to a level that did not differ from the control group (17 healthy older adults) [8]. Compared to aMCI memory performance under placebo, performance in the three-choice memory task was significantly improved with levetiracetam.

Elderly with cognitive impairment and seizures: BENEFIT. In an open-label prospective phase 4 study in 24 elderly patients with cognitive impairment and seizures, levetiracetam treatment (250 mg twice daily at first, then increased to final dose between 250 and 1500 mg twice daily) for 12 weeks significantly improved cognitive functions as measured by Mini Mental State Examination (MMSE) and the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) [9]. MMSE scores improved by an average of 2.2 points after 12 weeks. The expected decline over 3 months in this population was 1 point. Improvement for the delayed recall portion of MMSE was 0.6 points (on 3-word recall). ADAS-Cog scores improved by an average of 4.3 points. No significant changes were seen in behavioral or functional measures. There was little change in caregiver-reported behavior and function and no significant change in the activities of daily living (ADL) scale.

Children with autism and subclinical epilepsy: BENEFIT. In a prospective randomized controlled trial in 70 children with autism and subclinical epileptiform discharges, levetiracetam treatment (60 mg/kg/day) combined with educational training for 6 months normalized electroencephalographic measures while significantly improving behavioral and cognitive functions as measured by autism scores (CARS and ABC) [10]. The differences were significant compared to the control group which received educational training but no medications.

Brain tumor patients: POTENTIAL BENEFIT. In a cohort study of 117 patients with high-grade glioma, those who were on levetiracetam performed better on verbal memory tests than patients not on an anti-epileptic drug [11]. No differences were found for other cognitive functions, such as attention, executive function, working memory, psychomotor function, and information processing speed.

Human research to suggest benefits to patients with dementia:

Alzheimer's patients: UNKNOWN. In a double-blind controlled feasibility study in mild Alzheimer's patients (MMSE scores between 20-29), a single dose of levetiracetam (2.5 or 7.5 mg/kg, i.v.) did not alter cognitive performance [12]. The pattern of EEG data (decreased coherence in the lower frequency bands and increased coherence in the higher frequency bands) suggested a beneficial effect of levetiracetam in these patients, though at the time of publication, only 9 patients had been enrolled. Larger longitudinal studies and studies with healthy age-matched controls are needed to determine whether this represents a relative normalization of EEG patterns, whether it is unique to Alzheimer's as compared to normal aging, and whether longer term administration is associated with a beneficial clinical effect. Clinical trials in Alzheimer's patients are currently ongoing (NCT03489044, NCT02002819).

Alzheimer's patients with epilepsy: BENEFIT. A 2016 Cochrane report only found 1 randomized controlled trial including 95 Alzheimer's patients with epilepsy [13; 14]. This study showed that levetiracetam treatment (started at 500 mg/day, then increased weekly by 500 mg) for 12 months improved attention and oral fluency. At 12 months in the levetiracetam group, 27/38 (71%) were responders, 11 of whom (29%) had become seizure-free and 16/38 had a greater than 50% reduction in seizure frequency. MMSE scores in the levetiracetam group improved by a mean of 0.23 points compared to baseline; similar improvement was seen in ADAS-cog scores. There was no placebo control—the control group had Alzheimer's without epilepsy, and drug comparators were phenolbarbital and lamotrigine.

Dementia with manic behavior: UNKNOWN. In an open-label pilot trail of 19 geriatric patients with dementia and manic behavior, levetiracetam treatment (average of 592 mg daily) for ~12 days significantly improved mania scores but the treatment duration was too short to expect any changes in cognitive functions [15].

Lewy body dementia: UNKNOWN. It is not known whether levetiracetam has cognitive benefits in people with Lewy body dementia. There was a case report of a man with Lewy body dementia who had dream enactment behavior [16]. According to his wife, the frequency of nocturnal episodes decreased from 6 times to 3 times per month after levetiracetam treatment (1,000 mg twice daily). Concurrent medications included atorvastatin, escitalopram, aspirin, fexofenadine, folate, and vitamin B12. The patient was advised to taper off levetiracetam, at which point severity and frequency of nocturnal episodes increased again to 8 times per month.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:
It is thought that low-dose levetiracetam can selectively reduce aberrant, but not basal, neural activity, resulting in improved cognitive outcomes in preclinical and clinical studies [17].

fMRI studies: A study discussed above in amnestic MCI patients showed that levetiracetam normalizes the hyperactivity in hippocampal regions [7]. In a retrospective fMRI study in drug-resistant temporal lobe epilepsy patients, levetiracetam also showed restoration of normal activation patterns in the temporal lobe in a dose-dependent manner [18]. Longitudinal studies are needed to establish whether the neural patterns translate to drug response [19].

Molecular mechanisms of action: The exact molecular mechanism of action for levetiracetam is unknown. Levetiracetam has high affinity for the presynaptic membrane protein SV2A, which is widely expressed throughout the brain including high levels in the hippocampus [1; 17]. While the role of SV2A in biological function is not completely understood, it appears to play a role in modulating calcium-dependent neurotransmitter release by multiple mechanisms with a greater effect during high activation. SV2A influences neurotransmitter release via expression and trafficking of the calcium sensor synaptotagmin and likely binds directly to synaptotagmin. SV2A also contributes to the mobilization of synaptic vesicles for release, and SV2A deletion reduces vesicle release during trains of action potentials but does not measurably affect steady-state activity. Levetiracetam binding to SV2A is likely a primary mechanism of action for its anti-epileptic effects based on the strong linear correlation between affinity to SV2A and the ability to protect against seizures in a mouse model of audiogenic seizure [1].

In addition to mechanisms for quieting overactive neurons by limiting transmitter release, levetiracetam inhibits both ryanodine and IP3 receptor-activated calcium release in hippocampal neurons [20; 21], which would be neuroprotective in the context of impaired calcium homeostasis in Alzheimer's [22; 23].

Other evidence includes beneficial effects of levetiracetam on mitochondria. SV2A is also expressed in mitochondria and levetiracetam reduces mitochondrial swelling after calcium-induced and toxin (atractyloside)-induced opening of the mitochondrial permeability transition pore (mPTP) [24].

Levetiracetam may also act on astrocytic SV2A. In a human astrocyte culture study, levetiracetam inhibited Aβ-induced vesicular glutamate release and thus may underlie, at least in part, the ability of levetiracetam to reduce hyperexcitability in Alzheimer disease [25].

Models of Alzheimer's disease: Levetiracetam has shown benefit in several mouse models of Alzheimer's disease.

In the APPswe/PS1dE9 mice, levetiracetam (50 mg/kg, i.p.) alleviated behavioral deficits and reduced amyloid plaques while increasing Aβ clearance and up-regulating Aβ transport and autophagic degradation [26]. Levetiracetam also inhibited Aβ generation, suppressed γ-secretase activity, and inhibited GSK-3β activation, while increasing AMPK/Akt activation. Levetiracetam also inhibited histone deacetylase activity *in vivo*.

In the hAPPJ20 mice, levetiracetam reduced abnormal spike activity detected by EEG, and reversed hippocampal remodeling, behavioral abnormalities, synaptic dysfunction, and deficits in learning and memory [27]. However, prolonged levetiracetam treatment did not alter Aβ levels in the hippocampus. Levetiracetam did not improve these measures in normal mice.

In contrast to benefits observed in the studies above, levetiracetam treatment (10-20 mg/kg) was not able to rescue memory deficits in 5XFAD transgenic mice harboring amyloid plaque pathologies at moderate (6-8 months) or high (12-15 months) levels [28]. This was in contrast to levetiracetam ameliorating memory impairments of aged C57BL/6 mice (17-20 months) in the contextual fear conditioning paradigm. Acute levetiracetam immediately after training was also efficacious in rescuing contextual memory decline in aged mice, whereas administration at a later post-training interval (3 hours) had no effect.

APOE4 interactions: Unknown.

Aging and related health concerns: Although a few case studies suggested relief from peripheral neuropathy, a meta-analysis failed to find significant effects.

Types of evidence:

- 2 meta-analyses or systematic reviews, 1 in neuropathic pain and 1 in brain tumor patients
- 2 observational studies
- 1 case study of 3 patients with neuropathic pain
- Numerous laboratory studies

Neuropathy: MIXED/POTENTIAL BENEFIT. In a Cochrane meta-analysis of 6 double-blind randomized controlled trials with a total of 344 patients with neuropathic pain, there was insufficient data to conclude whether levetiracetam (2,000-3,000 mg/day) was effective in reducing neuropathic pain [29]. This was partly due to the outcome measures used, which were mostly subjective (e.g., participant-reported pain relief, Global Impression of Change). Also, this meta-analysis included patient populations of different types of neuropathic pain: central pain due to multiple sclerosis, pain following spinal cord injury, painful polyneuropathy, central post-stroke pain, post-herpetic neuralgia, and post-mastectomy pain. It is not known whether levetiracetam may be beneficial in some or all types of neuropathy.

In a case study of 3 patients with neuropathic pain, levetiracetam treatment significantly improved pain symptoms [30]. A 55-year-old woman with bilateral sensorimotor peripheral neuropathy with axonal and demyelinating features responded to 1,500 mg twice daily levetiracetam plus nortriptyline; her pain was improved by 60%. A 75-year-old man with numbness and persistent pain in both feet for 5 years experienced complete resolution of pain with a single dose of 500 mg levetiracetam. In a 67-year-old obese male with bilateral sensorimotor peripheral neuropathy with axonal and demyelinating features, treatment with levetiracetam (1,000 mg twice daily) resulted in complete elimination of pain.

Studies in preclinical models of peripheral neuropathy also suggest benefit with levetiracetam. In a mouse model of diabetes-induced peripheral neuropathy with sciatic degeneration, levetiracetam (40 mg/kg, oral) decreased pain sensitivity while decreasing spinal expression of microglia and astrocytes [31]. In another study in a mouse model of painful diabetic neuropathy, levetiracetam (10-100 mg/kg) produced anti-nociceptive effects and the combination of levetiracetam with aspirin, ibuprofen, or paracetamol produced further benefit, suggesting synergism between levetiracetam and ibuprofen/aspirin/paracetamol in this model [32]. In a rat model of diabetic neuropathy, treatment with levetiracetam (300 or 600 mg/kg, i.p.) significantly attenuated inflammation and fibrosis in sciatic nerves

and suppressed the increases in apoptosis markers (bax, caspase 3, caspase 8) and prevented the reduction in NGF expression [33].

Atherosclerosis: POTENTIAL HARM/MIXED. In a prospective longitudinal study of 109 patients with epilepsy, levetiracetam treatment (500 mg/day initially, then increased to reach maximal tolerable dose with good seizure control) for 6 months significantly increased LDL-C (from 90.2 to 98.5 mg/dl; 9.2% increase), homocysteine (from 7.9 to 10.4 µm; 31.6% increase), apolipoprotein B (from 63.6 to 77.4 mg/dl; 21.7% increase), and apolipoprotein B/A1 ratio (from 0.51 to 0.61) [34]. There were no significant changes in total cholesterol, triglyceride, HDL-C, lipoprotein(a), or vitamin B12. These findings suggest that treatment with levetiracetam might be associated with alterations in circulatory markers of vascular risk, which could contribute to the acceleration of atherosclerosis and increased risk of vascular diseases. The possible increase in atherogenecity associated with levetiracetam is not dependent on the CYP system or deficient cofactors for homocysteine metabolism (B12, etc.) and remains to be elucidated.

In contrast to the above findings, in an observational study of medical records including 2,144 patients with cerebral infarction (of whom 150 developed epilepsy), levetiracetam treatment did not alter total cholesterol, LDL-C, HDL-C, or triglyceride levels—levels were neck-to-neck to those of controls (untreated) [35]. They did find that other anti-epileptics such as carbamazepine and phenytoin significantly increased serum total cholesterol and LDL-C levels compared to baseline and untreated controls.

Safety: Numerous clinical trials have found that levetiracetam is well-tolerated but is associated with somnolence, fatigue, dizziness, irritability, and nasopharyngitis/infections. There are major drug interactions with pain killers and caffeine.

Types of evidence:

- 4 meta-analyses including 2 Cochrane meta-analyses
- 2 randomized controlled clinical trials
- 5 open-label trials
- 1 case study

Clinical studies: Numerous meta-analyses have examined the adverse events resulting from levetiracetam, though most studies have been in patients with epilepsy/seizures.

The most informative was a 2015 meta-analysis of 26 randomized controlled trials including 2,832 patients that was specifically focused on outcomes related to safety and adverse events [36]. Doses ranged from 1,000-4,000 mg/day, with most studies testing 3,000 mg/day. Treatment durations ranged from 6-24 weeks. Somnolence, asthenia/fatigue, dizziness, nervousness/irritability, and nasopharyngitis were significantly associated with levetiracetam treatment. In addition, levetiracetam was significantly associated with an increased risk of adverse event-related withdrawals. However, no dose-response relationship was found for any of the assessed variables.

In epilepsy/seizure patients: A 2012 Cochrane meta-analysis of 11 randomized controlled trials including 1,861 subjects with drug-resistant focal epilepsy also reported that levetiracetam (add-on therapy of 1,000-4,000 mg/day in adults, 60 mg/kg/day in children) treatment for 12-24 weeks was associated with increased incidences in somnolence (RR=1.51; 99% CI 1.06 to 2.17) and infection (RR=1.76; 99% CI 1.03 to 3.02) in adults [2]. No adverse effect was significantly associated with levetiracetam in children, but changes in behavior were observed, including hostility, nervousness, aggression, agitation, irritability, "abnormal behavior", altered mood, and anxiety. The 5 most common adverse effects (any age) were: somnolence: affected 14% of subjects (RR=1.58; 99% CI 1.14 to 2.18); headache: affected 10% of subjects (RR=0.95; 99% CI 0.65 to 1.39); fatigue (asthenia): affected 8% of subjects (RR=1.53; 99% CI 0.98 to 2.38); accidental injury (lower incidence with levetiracetam): affected 8% of subjects (RR=0.72; 99% CI 0.49 to 1.06); dizziness: affected 7% of subjects (RR=1.63; 99% CI 0.99 to 2.66). In adults, only the RRs for somnolence (RR=1.51; 99% CI 1.06 to 2.17) and infection (RR=1.76; 99% CI 1.03 to 3.02) remained statistically significant with levetiracetam over placebo.

In neuropathic pain patients: In a 2014 Cochrane meta-analysis in patients with neuropathic pain, the amount of data was limited (6 double-blind randomized controlled trials with 344 subjects total), but significantly more subjects experienced an adverse event with levetiracetam compared to placebo [29].

In Alzheimer's patients: In a randomized controlled trial of 95 patients with seizures and Alzheimer's disease, patients on levetiracetam therapy (500 mg/day initially, increased every week by 500 mg/day) reported mainly central nervous system-related and mild adverse events [14]. None of the patients had clinically significant changes from baseline in hematological, urinary, and biochemical parameters. There was no evidence of idiosyncratic side effects. Adverse effects, including somnolence (2), asthenia (2), headache (1), and dizziness (1), were observed in 6 (17%) patients. However, in general, tolerability was favorable, with transient adverse effects. No adverse events required discontinuation of treatment. No patients withdrew because of side effects.

In a prospective open-label study of 25 patients with advanced Alzheimer's and late-onset seizures, 16% discontinued from levetiracetam treatment (1,000-1,500 mg/day) due to adverse events, though the types of events were not discussed [37].

In elderly patients with epilepsy: In a randomized unblinded superiority study testing levetiracetam and other antiepileptics in 308 elderly patients with newly diagnosed epilepsy, adverse events were reported by 76.2 patients treated with levetiracetam [38]. Discontinuation rates due to adverse events were 11.3%. Higher severe adverse events were reported in the levetiracetam (20.5%) and carbamazepine (17.5%) groups compared to those treated with sodium valproate (8.2%). The most common adverse events were fatigue (11.3%) with levetiracetam.

In a small open-label phase 4 prospective study, 24 elderly patients with cognitive impairment and seizures were treated with levetiracetam (250 mg twice daily at first, then increased every 3 days until desired dose) for 12 weeks, and fatigue was the most common side effect (20.8%; 5 participants) [9]. One subject experienced loss of balance and dizziness but did not discontinue levetiracetam. There were no reports of insomnia, headache, anorexia, or weight loss.

In patients with brain tumors and seizures: In a prospective open-label study of 20 patients with brain tumors and seizures, levetiracetam (500 mg i.v. twice daily following surgery, then titrated by 500 mg/day increments up to a max dose of 3,000 mg/day) treatment was safe and well tolerated with no medication discontinuation during the study period [39]. Adverse effects reported were somnolence, nausea/vomiting, headache, and insomnia.

Case study of levetiracetam overdose: There was one case study of a 43-year-old female who overdosed with 60-80 grams of levetiracetam (along with 20 tablets of paracetamol/codeine and unknown quantity of alcohol) [40]. She experienced mild central nervous system depression, bradycardia, hypotension (86/57), and oliguria (low production of urine). Her cardiovascular toxicity transiently responded to atropine and intravenous fluids. An echocardiogram demonstrated normal left and right ventricular contractility. Despite her cardiovascular toxicity and oliguria, she had normal serial venous lactates and renal function, and made a complete recovery over 48 hours. Her levetiracetam concentration was 463 µg/ml 8 hours post-ingestion (therapeutic range 10-40 µg/ml). Levetiracetam in large amounts appears to cause bradycardia and hypotension that is potentially responsive to atropine and intravenous fluids. Based on a normal echocardiogram, levetiracetam at high concentration may have acted at muscarinic receptors.

Treato.com: Treato.com gives levetiracetam 3.8 stars out of 5. There are 149 positive comments and 109 negative ones. Concerns raised included depression (160), dizziness (112), nausea (88), drowsiness (75), and bipolar disorder (63).

Drug interactions: Levetiracetam has major drug interactions with 7 drugs: acetaminophen, aspirin, caffeine, buprenorphine, naloxone, propoxyphene (narcotic pain-reliever), and sodium oxybate (treatment for narcolepsy) (Drugs.com). It also has moderate drug interactions with 522 drugs (Drugs.com).

Sources and dosing: Levetiracetam is a prescription medication and comes in tablet (250, 500, 750, and 1,000 mg) and solution (500 mg/mL, 100 mg/mL) forms. Doses are started low (e.g., 250 mg twice daily), then increased until desired effect (e.g., seizure control) is achieved. Clinical studies in epilepsy patients have used doses ranging from 1,000-4,000 mg/day. In the ongoing clinical trial in Alzheimer's patients, a lower dose is being tested (500-1,000 mg/day)(NCT03489044).

Research underway: According to ClinicalTrials.gov, there are 21 clinical studies currently ongoing that are testing levetiracetam. Two clinical trials are investigating levetiracetam in Alzheimer's disease patients (NCT03489044, NCT02002819) and one study is testing levetiracetam in normal healthy adults who are APOE4 carriers (NCT03461861). Both Alzheimer's trials are scheduled to be completed in December 2019. Other clinical trials are testing levetiractam in patients with schizophrenia, seizures, brain tumors, and traumatic brain injury.

Search terms:
Pubmed, Google:

- + cognitive, + Alzheimer's, + APOE, + meta-analysis, + Cochrane, + lifespan, + cardiovascular, + neuropathy, + diabetes, + atherosclerosis

Websites visited for levetiracetam:

- Clinicaltrials.gov (36 studies ongoing)
- Examine.com (0)
- Treato.com
- DrugAge (0)
- Geroprotectors (0)
- Drugs.com
- WebMD.com

- PubChem
- DrugBank.ca
- Cafepharma (0)
- Pharmapro.com (0)

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