

Saliba's
Extended Care Pharmacy
A Guardian Pharmacy®

Dementia and Pharmaceuticals:

Things to Remember
When Caring for Those Who Forget

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OVERVIEW

DEFINE

Define dementia and provide background information



DISCUSS

Discuss dementia symptoms, diagnosis, and progression over time



DIFFERENTIATE

Differentiate between dementia and delirium



DESCRIBE

Describe different non-pharmacological and pharmacological treatment options

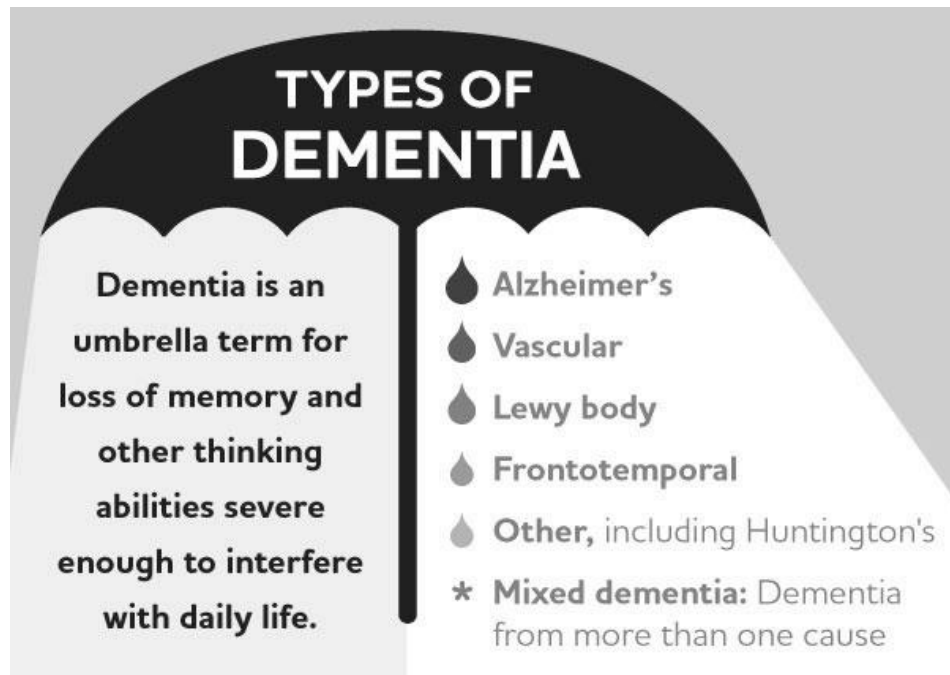


DELVE

Delve into details of prescription and OTC medications used for dementia, including use, side effects, and treatment goals

WHAT IS DEMENTIA?

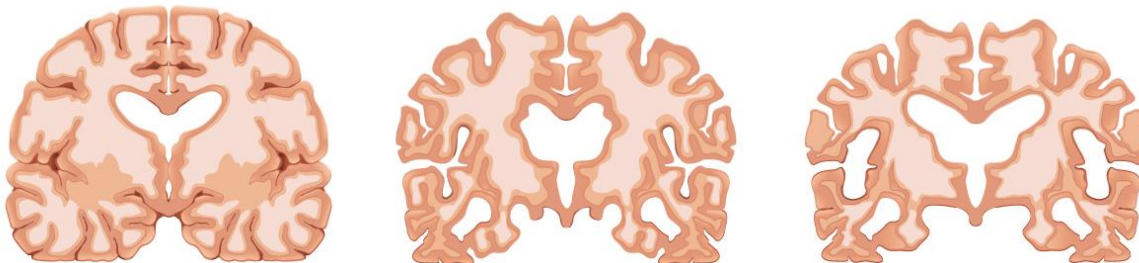
- Dementia is not a single disease – it is an umbrella term that describes a group of symptoms
- Can be caused by a wide variety of more specific medical conditions
- The most common cause of dementia is Alzheimer's disease
- Alzheimer's accounts for ~60-80% of dementia cases
- Specific cause for Alzheimer's disease is unknown.
- Not all medications approved to treat cognitive symptoms in Alzheimer's-related dementia are effective at treating other types of dementia (ex. frontotemporal dementia.)



DEMENTIA BACKGROUND

- There is a formerly widespread assumption that elderly mental decline (inaccurately described as elderly “senility”) is a normal part of aging. This assumption is FALSE.
- Dementia is caused by damage to brain cells/neurons, which interferes with communication between these cells
- Dementia affects memory, reasoning, behavior, emotions, and eventually bodily movement / physical functions
- It is not reversible and there is no cure
- The focus of treatment is on symptom management and slowing progression
- On average, those with Alzheimer’s disease live between 3-11 years after they are diagnosed, but there is no set timeline of progression. Some people may survive 20 years or more.

BRAIN CHANGES OVER TIME IN DEMENTIA



DEMENTIA vs DELIRIUM SYMPTOMS

DEMENTIA

- Unable to learn new information
- Wandering/pacing
- Appetite changes
- Gait changes / motor disturbances
- Poor drawing
- Difficulty recalling words

EITHER

- Anxiety
- Agitation
- Hallucinations
- Delusions
- Changes in behavior and/or emotions
- Memory dysfunction
- Sleep disturbances
- Symptoms worse at night

DELIRIUM

- Acute confusion
- Disorientation to time or place
- Impaired attention
- Altered level of consciousness
- Incoherent, rapid or
- Slurred speech

DIFFERENTIATING DELIRIUM VS DEMENTIA SYMPTOMS

- Delirium is a medical emergency that requires immediate treatment
- Most important distinguishing factor is the abrupt onset of delirium (rapid change in condition)

- **DELIRIUM CAUSES:**

- ✓ Infection (~58%)
- ✓ High or low blood sugar
- ✓ High or low sodium levels
- ✓ Dehydration
- ✓ Low blood oxygen
- ✓ Drug-induced

TABLE 2 – DIFFERENTIATING DELIRIUM FROM DEMENTIA

CHARACTERISTIC	DELIRIUM	DEMENTIA
Onset	Acute	Insidious
Course	Fluctuating	Gradual deterioration
Awareness	Impaired	Often clear until advanced stages
Attention	Disturbed	Often good until advanced stages
Memory	Poor working memory and immediate recall	Poor short-term memory
Delusions	Often short-lived or changing	More fixed
Sleep disturbances	Fragmented sleep	Sleep-awake reversal

DEMENTIA DIAGNOSIS


- Older adults with no symptoms are not routinely screened for cognitive impairment.
- There is no one single test to diagnose
- Referral to neurologist may be necessary to determine a specific diagnosis (Alzheimer's dementia, Lewy Body dementia, Parkinson's disease, etc.)
- Diagnosis is based on several factors including the following:
 - ✓ Medical history – cognitive and behavioral history from family members / caregivers
 - ✓ Physical examination
 - ✓ Laboratory tests
 - Screening for B12 deficiency and hypothyroidism is recommended for patients being evaluated for dementia
 - MRI or CT should be considered in initial evaluation of patients with dementia
 - ✓ Cognitive tests
 - Mini-Mental State Examination (MMSE)
 - Mini-Cog Test
 - Montreal Cognitive Assessment (MoCA)

DEMENTIA DIAGNOSIS TOOLS

Mini-Mental State Examination (MMSE)

Patient's Name: _____ Date: _____

Instructions: Ask the questions in the order listed. Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

(Adapted from Rovner & Folstein, 1987)

MINI-MENTAL STATE EXAMINATION (MMSE)

SCORE	DEGREE OF IMPAIRMENT	DAY-TO-DAY FUNCTIONING
25-30	Questionably significant	May have clinically significant but mild deficits. Likely to affect only most demanding activities of daily living.
20-25	Mild	Significant effect. May require some supervision, support and assistance.
10-20	Moderate	Clear impairment. May require 24-hour supervision.
0-10	Severe	Marked impairment. Likely to require 24-hour supervision and assistance with activities of daily living.

DEMENTIA DIAGNOSIS TOOLS

Mini-Cog®

Instructions for Administration & Scoring

ID: _____ Date: _____

Step 1: Three Word Registration

Look directly at person and say, "Please listen carefully. I am going to say three words that I want you to repeat back to me now and try to remember. The words are [select a list of words from the versions below]. Please say them for me now." If the person is unable to repeat the words after three attempts, move on to Step 2 (clock drawing).

The following and other word lists have been used in one or more clinical studies.^{1,9} For repeated administrations, use of an alternative word list is recommended.

Version 1	Version 2	Version 3	Version 4	Version 5	Version 6
Banana	Leader	Village	River	Captain	Daughter
Sunrise	Season	Kitchen	Nation	Garden	Heaven
Chair	Table	Baby	Finger	Picture	Mountain

Step 2: Clock Drawing

Say: "Next, I want you to draw a clock for me. First, put in all of the numbers where they go." When that is completed, say: "Now, set the hands to 10 past 11."

Use preprinted circle (see next page) for this exercise. Repeat instructions as needed as this is not a memory test. Move to Step 3 if the clock is not complete within three minutes.

Step 3: Three Word Recall

Ask the person to recall the three words you stated in Step 1. Say: "What were the three words I asked you to remember?" Record the word list version number and the person's answers below.

Word List Version: _____ Person's Answers: _____

Scoring

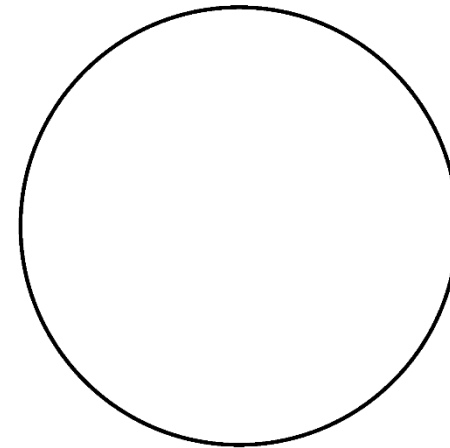
Word Recall: _____ (0-3 points)	1 point for each word spontaneously recalled without cueing.
Clock Draw: _____ (0 or 2 points)	Normal clock = 2 points. A normal clock has all numbers placed in the correct sequence and approximately correct position (e.g., 12, 3, 6 and 9 are in anchor positions) with no missing or duplicate numbers. Hands are pointing to the 11 and 2 (11:10). Hand length is not scored. Inability or refusal to draw a clock (abnormal) = 0 points.
Total Score: _____ (0-5 points)	Total score = Word Recall score + Clock Draw score. A cut point of <3 on the Mini-Cog™ has been validated for dementia screening, but many individuals with clinically meaningful cognitive impairment will score higher. When greater sensitivity is desired, a cut point of <4 is recommended as it may indicate a need for further evaluation of cognitive status.

MINI-COG

Clock Drawing

ID: _____

Date: _____



NON-PHARMACOLOGICAL THERAPY

NON-DRUG MEASURES AND HEALTHY HABITS THAT MAY IMPROVE COGNITION AND QUALITY OF LIFE FOR DEMENTIA PATIENTS

- Nutrition – dementia can possibly contribute to weight gain or weight loss
 - ✓ Decreased food intake, malnutrition, and failure to thrive are all more likely, especially in advanced stages of dementia
 - ✓ Mediterranean-like diet may reduce risk of cognitive decline
- Exercise programs – aerobic activity seems to provide more benefit than resistance training
- Cognitive rehabilitation / cognitive stimulation programs
- Stress management
- Proper sleep hygiene
- Occupational therapy
- Aromatherapy
- Music therapy
- Pet therapy
- Alcohol reduction or cessation
- Smoking cessation

NON-COGNITIVE SYMPTOM MANAGEMENT

4 “A”s OF BEHAVIORS: AGITATION, ANXIETY, ANGER, AGRESSION

- ≥80% of patients with Alzheimer’s Dementia (AD) will experience agitation
- ~40% of patients with AD will experience aggression.
- Use structured routines, distraction / redirection, calming and reassuring responses
- **ABC’s of assessing a behavior occurrence**
 - ✓ **A: ANTECEDENTS** (cause)
 - What triggered the behavior?
 - Assess for pain, environment issues, and other modifiable factors
 - ✓ **B: BEHAVIOR**
 - Describe what happened using objective, concrete descriptions
 - What is the frequency, duration, and severity of the behavior?
 - Is it a target for intervention?
 - ✓ **C: CONSEQUENCES**
 - What happened after the behavior? Was anyone injured?
 - For whom will there be consequences? (the patient or others)
 - Serious episodes can result in discharge to elevated level of care

PHARMACOTHERAPY FOR NON-COGNITIVE SYMPTOMS

MEDICATIONS FOR AGITATION, ANXIETY, DEPRESSION, AND OTHERS

- **ANTIDEPRESSANTS**

- ✓ Treatment for agitation, depression, psychosis, insomnia, anxiety, neuropathic pain

- **BUSPIRONE**

- ✓ Treatment for anxiety, mild to moderate agitation

- **ANTI-SEIZURE MEDICATIONS/ MOOD STABILIZERS** (carbamazepine, valproic acid, etc.)

- ✓ Treatment for agitation
- ✓ These may require additional lab monitoring / screening for drug interactions
- ✓ Valproic acid/divalproex and other mood stabilizer appear on the Beer Criteria as possibly inappropriate for older adults due to increased syncope (fainting) and impaired psychomotor function, and should be used with caution and monitoring.

- **DEXTROMETHORPHAN/QUINIDINE** (brand name: Nuedexta)

- ✓ Treatment for agitation in Alzheimer's dementia.
- ✓ Expensive (~\$1,425/month)



PHARMACOTHERAPY FOR COGNITIVE SYMPTOMS

■ CHOLINESTERASE INHIBITORS

- ✓ Donepezil (Aricept)
- ✓ Galantamine (Razadyne)
- ✓ Rivastigmine (Exelon)

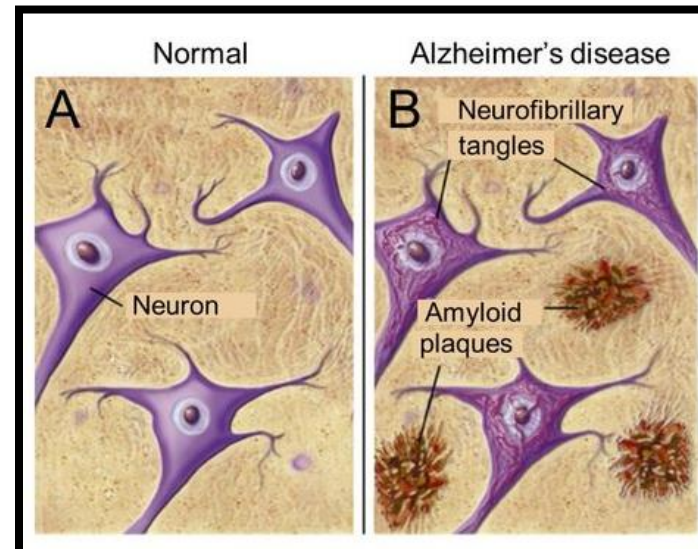
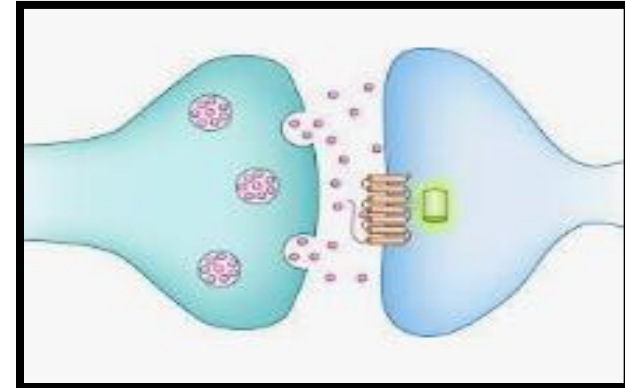
■ N-METHYL-D-ASPARTATE RECEPTOR ANTAGONISTS

- ✓ Memantine (Namenda)

■ MONOCLONAL ANTIBODY (amyloid targeting)

- ✓ Adacantumab (Aduhelm)

■ OTCS AND SUPPLEMENTS



PHARMACOTHERAPY FOR COGNITIVE SYMPTOMS

- **CHOLINESTERASE INHIBITORS - COMMON POSSIBLE SIDE EFFECTS (>1%):**
 - ✓ **GI (most common):** diarrhea, nausea, vomiting, loss of appetite/ weight loss, abdominal pain, dyspepsia
 - ✓ **CNS:** Dizziness, drowsiness, insomnia, confusion*, hallucinations*, depression, headache, tremor
 - ✓ **Cardiovascular:** bradycardia, hypertension
 - ✓ **Respiratory:** may worsen asthma / COPD
 - ✓ **Other:** fatigue, malaise, weakness, falls*
- ***SEVERE SIDE EFFECTS TO NOTIFY PHYSICIAN:**
 - ✓ Gastrointestinal bleeding, especially with NSAID use or history of peptic ulcer disease
 - ✓ Confusion, hallucinations, increased seizure activity
 - ✓ Fainting, falls
- Due to side effect profile of this class of drug, use of these medications should be regularly reassessed by the physician to decide if benefits continue to outweigh the risks, especially after a significant adverse event such as a fall. Adverse effects are most likely when starting or increasing doses.

PHARMACOTHERAPY: CHOLINESTERASE INHIBITORS

DONEPEZIL (ARICEPT)

▪ APPROVED USE:

- ✓ Alzheimer's disease - dementia (**MILD, MODERATE OR SEVERE**)

▪ HOW SUPPLIED:

- ✓ Oral tablets: 5mg, 10mg, 23mg*
- ✓ ODT tablets: 5mg, 10mg
- ✓ Transdermal 24hr patch (Adlarity): 5mg, 10mg

▪ RECOMMENDATIONS FOR TAKING / COUNSELING POINTS

- ✓ Typically started at 5mg, then increased to 10mg after 4-6 weeks
- ✓ Side effects may be more frequent after dose increases and tend to resolve with longer use
- ✓ It may be advised to take in the evening at bedtime to reduce likelihood of falls caused by dizziness. (Timing may be altered to be taken in the morning instead if it causes insomnia).
- ✓ May take with or without food
- ✓ *Doses higher than 10mg daily have limited data for increased efficacy and have increased likelihood of adverse effects.

PHARMACOTHERAPY: CHOLINESTERASE INHIBITORS

GALANTAMINE (RAZADYNE)

▪ APPROVED USE:

- ✓ Alzheimer's disease - dementia (**MILD TO MODERATE**)

▪ HOW SUPPLIED:

- ✓ ER capsule: 8mg, 16mg, 24mg- once daily dosing
- ✓ Oral solution: 4mg/mL – twice daily dosing
- ✓ Oral tablet: 4mg, 8mg, 12mg – twice daily dosing

▪ RECOMMENDATIONS FOR TAKING / COUNSELING POINTS

- ✓ Take with food to minimize gastric irritation / side effects.
- ✓ Maintain adequate hydration while on this medication
- ✓ If doses missed for more than 3 days, consult physician as drug will likely need to be restarted at lowest dose.

PHARMACOTHERAPY: CHOLINESTERASE INHIBITORS

RIVASTIGMINE (EXELON)

▪ APPROVED USE:

- ✓ Alzheimer's disease - dementia (**MILD TO MODERATE**)
- ✓ Parkinson's disease - dementia (**MILD TO MODERATE**)

▪ HOW SUPPLIED:

- ✓ 24-hour transdermal patch: 4.6 mg, 9.5mg, 13.3mg – 1 patch replaced every 24 hours, rotating application sites
- ✓ Recommended application sites: upper or lower back (less likely to be removed by patient), or upper arm or chest
- ✓ Oral capsule: 1.5mg, 3mg, 4.5mg, or 6mg taken twice daily

▪ RECOMMENDATIONS FOR TAKING / COUNSELING POINTS

- ✓ Possible skin irritation with transdermal patch – rotate application sites
- ✓ Do not cut patches
- ✓ Take capsules with meals (breakfast & dinner)
- ✓ If doses missed for several days, drug may need to be restarted at lower dose.

PHARMACOTHERAPY FOR COGNITIVE SYMPTOMS

- **NMDA RECEPTOR ANTAGONISTS (MEMANTINE) – COMMON POSSIBLE SIDE EFFECTS (>1%):**

- ✓ GI: Constipation, diarrhea, vomiting, weight gain
- ✓ CNS: confusion*, dizziness, drowsiness, headache, hallucinations*, anxiety, aggression, depression
- ✓ Cardiovascular: hypertension, hypotension
- ✓ Other: cough, dyspnea

- ***SEVERE SIDE EFFECTS TO NOTIFY PHYSICIAN:**

- ✓ CNS: confusion, hallucinations
- ✓ Dermatologic: Stevens-Johnson syndrome (rare: <1%)
- ✓ Fainting

PHARMACOTHERAPY

N-METHYL-D-ASPARTATE RECEPTOR ANTAGONISTS (NMDA INHIBITORS)

MEMANTINE (NAMENDA)

▪ APPROVED USE:

- Alzheimer's disease – dementia (**MODERATE TO SEVERE**)

▪ HOW SUPPLIED:

- ✓ Oral tablet: 5mg, 10mg
- ✓ Oral capsule (extended release): 7mg, 14mg, 21mg, 28mg
- ✓ Oral solution: 2mg/mL

▪ RECOMMENDATIONS FOR TAKING / COUNSELING POINTS

- ✓ Must be slowly titrated
- ✓ Typical titration schedules:
 - IR tablet: 5mg once daily x 1 week, then 5mg twice daily, then 5mg in the morning & 10mg in the evening, then 10mg twice daily
 - ER capsule: 7mg once daily x 1 week, then 14mg once daily x 1 week, then 21mg once daily x 1 week, then 28 mg once daily
- ✓ ER capsule may be opened and sprinkled on applesauce, but do not crush or chew the beads inside the capsule.

COMBINATION MEDICATION

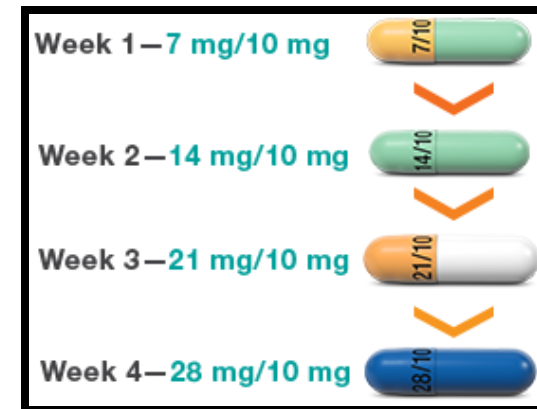
MEMANTINE + DONEPEZIL (NAMZARIC)

▪ APPROVED USE:

- Alzheimer's disease – dementia (**MODERATE TO SEVERE**)

▪ DOSING INFORMATION:

- ✓ Oral capsule (extended release):
- ✓ 7mg-10mg, 14mg-10mg, 21mg-10mg, 28mg-10mg
- ✓ For patients who are currently stabilized on donepezil and not taking memantine:
 - ✓ Start at lowest dose (7mg-10mg) and may be increased to next dose increment after at least 1 week.
- ✓ For patients who are currently stabilized on donepezil 10mg daily PLUS memantine 10mg twice daily or memantine ER 28mg daily:
 - ✓ May start at highest dose (28mg/10mg)



MONOCLONAL ANTIBODY

ADUCANUMAB-AVWA (ADUHELM)

- Approved in 2021 for treatment of Alzheimer's disease (early stage/ mild cognitive impairment)
- Eliminates clumps of toxic proteins called beta-amyloid plaques that are believed to destroy neurons in the brain.
- Does this by stimulating immune system to attack and break down those plaques.
- Administration: IV infusion over 1 hour once a month
- Side effects:
 - ✓ Painful brain swelling (35% to 41%), headaches (20%)
 - ✓ Confusion, delirium, disorientation, vision changes, diarrhea (8-9%)
 - ✓ Falls (15%)
 - ✓ Brain bleeding (0.5%), Seizures (0.5%)
- Cost without insurance: ~\$28,000 / year
 - ✓ 80% covered by some Medicare Part B plans – patient pays: ~\$5,600/year
- Additional costs: PET scan required before starting treatment and MRI scans before and during treatment

MONOCLONAL ANTIBODY

ADUCANUMAB-AVWA (ADUHELM)

- **CONTROVERSIAL USE:**
 - ✓ Evidence demonstrates it removes beta amyloid plaques but the trial data showed very small benefits in reduction of cognitive loss.
 - ✓ Many health institutions decline to offer this treatment due to perception of risks and costs outweighing benefits.



OVER-THE-COUNTER REMEDIES & SUPPLEMENTS

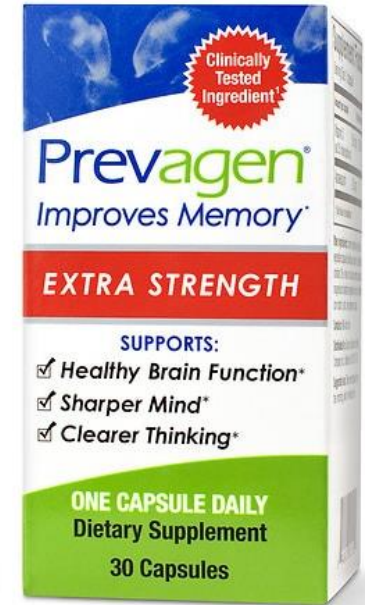
GINKO BILOBA

- Efficacy & Safety Classifications in Natural Medicines Database:
 - ✓ “POSSIBLY EFFECTIVE” (product has some clinical evidence supporting its use for this indication; however, the evidence is limited by quantity, quality, or contradictory findings)
 - ✓ “LIKELY SAFE” when taken orally and appropriately
- Drug interactions:
 - ✓ Anticoagulants/antiplatelets/warfarin/ibuprofen: increased risk of bleeding
 - ✓ Anticonvulsants: decreased effectiveness
 - ✓ Some statins (cholesterol medications): possible decreased effectiveness
 - ✓ Insulin: Ginko biloba may alter function of pancreas and therefore adjustment of insulin may be necessary
 - ✓ Nifedipine: increased plasma concentrations of nifedipine, possible hypotension

OVER-THE-COUNTER REMEDIES & SUPPLEMENTS

PREVAGEN

- Main ingredients per capsule:
 - ✓ Vitamin D3 50mcg
 - ✓ Apoaequorin 20mg
- Other Ingredients:
 - ✓ Microcrystalline Cellulose, Vegetable Capsule (Form: Cellulose, Water), Sugar, Contains 2% or less of: (Form: Acacia (Alt. Name: Gum Arabic) Genus: Acacia, Casein Peptones, Corn Starch, DL-Alpha-Tocopherol, Lactose, Magnesium Stearate Note: vegetable source, Medium Chain Triglycerides Note: vegetable oil, Salt, Soy Peptones, Tricalcium Phosphate, Water)
- Recommendation for use:
 - ✓ As with many supplements, there is insufficient data to recommend for or against use of Prevagen. Use caution with supplements and any claims made/ implied for efficacy as they are not regulated by FDA.



MEDICATIONS THAT POSE INCREASED RISKS FOR PATIENTS WITH DEMENTIA

MEDICATIONS WITH ANTICHOLINERGIC EFFECTS:

- Possible decreased efficacy of cholinesterase inhibitors (ex. donepezil)
- Increased risk of dementia, delirium, confusion, hallucinations
 - ✓ Antihistamines (diphenhydramine, doxylamine)
 - ✓ Overactive bladder medications (oxybutynin, tolterodine, solifenacin)
 - ✓ Gastrointestinal agents (dicyclomine, meclizine, promethazine)
 - ✓ Muscle relaxants (cyclobenzaprine, baclofen, methocarbamol, tizanidine)
 - ✓ Tricyclic antidepressants (amitriptyline, nortriptyline)
 - ✓ Some antipsychotics (clozapine)
 - ✓ Some antidepressants (paroxetine)
 - ✓ Parkinson's drugs (benztropine, trihexyphenidyl)
 - ✓ Others

MEDICATIONS THAT POSE INCREASED RISKS FOR PATIENTS WITH DEMENTIA

ANTIPSYCHOTICS:

- All antipsychotics carry FDA black box warning for use in elderly patients with dementia due to increased risk for stroke, cognitive decline, and death.
- May worsen delirium, unsteady gait, psychomotor impairment, syncope, and fall risk.
- Antipsychotic use is acceptable for treatment of dementia-related behavioral problems only if the patient is considered a risk to themselves or others.
 - ✓ Use lowest effective dose for shortest time possible, and there should be frequent re-evaluation and attempts of gradual dose reduction / discontinuation where possible.
- **Antipsychotics and other medication should never be used as a chemical restraint** (e.g., for discipline or staff convenience).

MEDICATIONS THAT POSE INCREASED RISKS FOR PATIENTS WITH DEMENTIA

BENZODIAZEPINES

- Increased risk of dementia, delirium, worsening cognition
- Use alternatives for anxiety (buspirone or SSRIs)
- Avoid use with opioids and other sedating medications

SLEEP AIDS (“Z” DRUGS – ZOLPIDEM, ESZOPICLONE, ZALEPLON)

- Increased risk for dementia, delirium, worsening cognition
- Avoid use with opioids and other sedating medications

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