RIVASTIGMINE

THERAPEUTICS

Brands
• Exelon, Prometax

Generic?
No

Class
• Cholinesterase inhibitor

Commonly Prescribed for
(FDA approved in bold)
• Alzheimer dementia (AD) (mild or moderate)
• Dementia associated with Parkinson’s Disease (PD)
• Dementia with Lewy Bodies (DLB)
• Vascular dementia

How the Drug Works
• Increases the concentration of acetylcholine through reversible inhibition of acetylcholinesterase, which increases availability of acetylcholine. Also inhibits butyrylcholinesterase. A deficiency of cholinergic function is felt to be important in producing the signs and symptoms of AD. May interfere with amyloid deposition
• Although symptoms of AD can improve, rivastigmine does not prevent disease progression

How Long Until It Works
• Typically 2–6 weeks at a given dose, but effect is best observed over a period of months

If It Works
• Continue to use but symptoms of dementia usually continue to worsen

If It Doesn’t Work
• Non-pharmacologic measures are the basis of dementia treatment. Maintain regular schedules and routines. Avoid prolonged travel, unnecessary medical procedures or emergency room visits, crowds, and large social gatherings
• Limit drugs with sedative properties such as opioids, hypnotics, antiepileptic drugs and tricyclic antidepressants

Best Augmenting Combos for Partial Response or Treatment-Resistance
• Addition of the NMDA receptor antagonist memantine may be beneficial
• Treat depression or apathy, if present, with SSRIs. Avoid tricyclic antidepressants in demented patients due to risk of confusion
• For significant confusion and agitation avoid typical neuroleptics (especially in DLB) because of the risk of neuroleptic malignant syndrome. Atypical antipsychotics (risperidone, quetiapine, olanzapine, clozapine) can be used instead

How Drug Causes AEs
• Acetylcholinesterase and butyrylcholinesterase inhibition in the CNS and PNS

Notable AEs
• GI AEs (nausea/vomiting, diarrhea, anorexia, increased gastric acid secretion and weight loss) are most common
• Fatigue, depression, dizziness, increased sweating and headache

Life-Threatening or Dangerous AEs
• Rarely bradycardia or heart block causing syncope. Generalized convulsions. Increases gastric acid secretions which can predispose to GI bleeding

Weight Gain
• Unusual

Sedation
• Unusual

ADVERSE EFFECTS (AEs)

Tests
• None required
What to Do About AEs
- In patients with dementia, determining if AEs are related to medication or another medical condition can be difficult. For CNS side effects, discontinuation of non-essential centrally acting medications may help. If a bothersome AE is clearly drug-related then lower the dose (especially for GI AEs), titrate more slowly or discontinue

Best Augmenting Agents for AEs
- Most AEs do not respond to adding other medications

DOSING AND USE

Usual Dosage Range
- 6–12 mg/day in 2 divided doses for oral formulations, or 4.6 or 9.5 mg 1 transdermal patch per day

Dosage Forms
- Capsules: 1.5, 3, 4.5 and 6 mg
- Oral solution: 2 mg/mL in a 120 mL bottle
- Patches: 4.6 mg/24 hour and 9.5 mg/24 hour

How to Dose
- Start at 1.5 mg twice a day. Increase at a minimum of 2 weeks by 3 mg/day to a maximum of 12 mg/day in 2 divided doses
- Transdermal patch: start 4.6-mg/24-hour patch applied once daily. After 4 weeks increase to one 9.5-mg/24-hour patch daily if well-tolerated

Dosing Tips
- Slow titration can reduce AEs. Nausea is most common in the titration phase. Food slows absorption

Overdose
- Symptoms of cholinergic crisis can occur: nausea/vomiting, salivation, hypotension, diaphoresis, convulsions, bradycardia/collapse. May cause muscle weakness and respiratory failure. Atropine with an initial dose of 1–2 mg IV is a potential antidote

Long-Term Use
- Safe for long-term use. Effectiveness may decrease over time as the dementing illness progresses

Habit Forming
- No

How to Stop
- Abrupt discontinuation can produce worsening of dementia symptoms, memory and behavioral disturbances. Taper slowly

Pharmacokinetics
- Elimination half-life 1–2 hours. No hepatic interactions or CYP-450 interactions. Metabolites are excreted in urine

Drug Interactions
- Increases the effect of anesthetics such as succinylcholine. Stop before surgery
- Anticholinergics interfere with effect of drug
- Other cholinesterase inhibitors and cholinergic agonists (bethanechol) may cause a synergistic effect
- Bradycardia may occur when used with beta-blockers
- Nicotine increases drug clearance

Do Not Use
- Known hypersensitivity to the drug or carbamate derivatives

SPECIAL POPULATIONS

Renal Impairment
- Variable changes in clearance with moderate and severe disease. No dose adjustment needed

Hepatic Impairment
- Patients with severe disease have 60% reduced clearance but not clinically significant. No dose adjustment needed

Cardiac Impairment
- Syncope has been reported

Elderly
- No known effects

Children and Adolescents
- Not studied. AD does not occur in children
RIVASTIGMINE

Pregnancy
• Category B. Use only if benefits of medication outweigh risks

Breast Feeding
• Unknown if excreted in breast milk. Do not use

THE ART OF NEUROPHARMACOLOGY
Potential Advantages
• Proven effectiveness for AD and PD dementia. Low risk of the hepatotoxicity seen with other acetylcholinesterases (tacrine) and fewer drug interactions than donepezil. Available as a transdermal patch. Additional inhibition of butyrylcholinesterase may increase effectiveness

Potential Disadvantages
• Cost and minimal effectiveness. Does not prevent progression of AD or other dementia. GI AEs

Primary Target Symptoms
• Confusion, agitation, memory, performing activities of daily living

Pearls
• May be used in combination with memantine with good effect, but combining with other cholinesterase inhibitors is not recommended
• In most clinical trials, medication treatments for AD patients had a similar rate of benefit
• May be useful for both behavioral problems in AD (delusion, anxiety and apathy for example) as well as memory disturbance
• PD patients may benefit from lower doses than in AD (less than 6 mg/day)
• Usually the effect of rivastigmine is not dramatic, but patients with DLB might show more benefit. Effective for the cognitive and behavioral symptoms (agitation, apathy, hallucinations) of DLB
• When changing from one cholinesterase inhibitor to another, avoid a washout period which could precipitate clinical deterioration
• Butyrylcholinesterase inhibition may be more beneficial in later stages of AD when gliosis occurs
• May be more selective for the form of acetylcholinesterase in the hippocampus (G1)

Suggested Reading


