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DUR DIGEST

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Drugs for Dementia

Dementia comes in many different forms, with Alzheimer's disease (AD) being the most common. Acetylcholinesterase inhibitors (donepezil, galantamine, rivastigmine and tacrine) inhibit the enzyme that breaks down acetylcholine, thus increasing its concentration in the brain, which may have a beneficial effect on the symptoms of dementia. Acetylcholinesterase inhibitors carry with them a common adverse effect profile seen with cholinergic medications, such as bradycardia, syncope, nausea, vomiting and diarrhea. These adverse effects seem to be most common with initiation of therapy and when the dose is increased. The mechanism of action for the *N*-methyl-D-aspartate (NMDA)-receptor antagonist, memantine, is unknown. It is postulated that it blocks the amino acid glutamate, which contributes to the symptoms of AD. Common adverse effects include dizziness, confusion, hallucinations, delusions and insomnia.

The acetylcholinesterase inhibitors, Aricept® (donepezil) and Exelon® (rivastigmine), and the NMDA-receptor antagonist ,Namenda® (memantine), currently do not require a Prior Authorization but are restricted to patients 40 years of age and older.

Aricept® (donepezil) is FDA approved for treatment of mild-to-moderate AD, Exelon® (rivastigmine) is FDA approved for treatment of mild to moderate dementia associated with AD or Parkinson's disease, and Namenda® (memantine) is FDA approved for the treatment of moderate-to-severe AD. Although FDA approved for Alzheimer's, additional studies performed have questioned these drugs' efficacy. A meta-analysis published by Raina et al reviewed 20 years of English language randomized, controlled trials evaluating all cholinesterase inhibitors and memantine. A total of 96 publications and 59 discrete studies were included in this review. Their conclusions were that all agents used to treat dementia provide statistically significant yet clinically marginal outcomes in terms of improved cognition.[2] A 2008 clinical practice guideline co-authored by the American College of Physicians and the American Academy of Family Physicians, reviewed the current five drug treatment options for dementia. In addition to reporting results on the statistical significance of trials, the guideline panel assessed clinically important effects of treatment regimens, as measured by generally-accepted magnitudes of changes in tools used to measure cognition defects. As in Raina's review, the guideline panel found statistical significance without uniform clinical significance, and lack of convincing evidence demonstrating superiority of one therapeutic treatment over another.[3]

When prescribing these medications, consideration must be given to the significant cost of the medication and the adverse effects caused by these medications. If patients have not responded to therapy three months after initiation of therapy, the medication should be stopped. It should also be noted that these medications do not stop or reverse the progression of AD.

References:

1. American Psychiatric Association Diagnostic and Statistical Manual, 4th ed, APA Press, Washington DC, 1994.
2. Raina P, Santaguida P, Ismaila A et al. Effectiveness of cholinesterase inhibitors and memantine for treating dementia: evidence review for a clinical practice guideline. *Ann Intern Med* 2008 Mar 04; 148(5): 379-97.
3. Qaseem A, Snow V, Cross JT Jr et al. Current pharmacologic treatment of dementia: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med* 2008 Mar 04; 148(5):370-78.

Type 2 diabetes is a chronic condition that can lead to a great deal of individual suffering and economic loss. However, much of the morbidity associated with the long term microvascular and neuropathic complications can be avoided with tight glycemic control.

In early 2009, the American Diabetes Association (ADA) as well as the American Diabetes Association and the European Association for the Study of Diabetes (ADA/EASD) updated their consensus guidelines for treating type 2 diabetes. The consensus algorithm from the ADA/EASD has two treatment tiers; Tier 1 is “well-validated core therapies” which includes metformin + lifestyle as step 1, and metformin + lifestyle + basal insulin or a sulfonylurea as step 2, and metformin + lifestyle + intensive insulin as step 3. Tier 2 is considered “less well-validated therapies” and includes pioglitazone and GLP-1 agonists as alternatives. The guideline states that amylin agonists, α-glucosidase inhibitors, glinides, and DPP-4 inhibitors are not included in the two tiers of preferred agents in the treatment algorithm due to their lower or equivalent overall glucose-lowering effectiveness compared with the first and second-tier agents and/or to their limited clinical data. However, these agents may be appropriate in selected patients. [1, 2]

In addition, it is well established that self blood glucose monitoring in type 2 diabetics who are not using insulin is not cost effective. A trial published in the British Medical Journal in 2008 looked at the cost effectiveness of self monitoring of blood glucose in type 2 diabetics who were not using insulin. The data for this trial came from the randomized controlled diabetes glycemic education and monitoring (DiGEM) trial which looked at 12 months of data before the baseline and 12 months of trial follow up data. This study concluded that self monitoring of blood glucose with or without additional training in incorporating the results into self care was associated with higher costs and lower quality of life in patients with non-insulin treated type 2 diabetes.[3] Similar results from different studies were recently published in the Canadian Medical Association Journal. The 2010 American Diabetes Association *Standards of Medical Care in Diabetes* states that the optimal frequency and timing of self blood glucose monitoring for patients with type 2 diabetes who are not using insulin is unclear.[4]

References:

1. Nathan DM, Buse JB, Davidson MB, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2009 Jan;32 193-203**.**

2. American Diabetes Association. Standards of medical care in diabetes—2009 [guideline on the Internet]. Diabetes Care. 2009 Jan [cited 2009 Dec 17];32 Suppl 1:S13-61.

3. Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. BMJ (clinical research ed.); 2008 May 336 7654, 1177 (1177-80).

4. American Diabetes Association. Standards of medical care in diabetes – 2010 [guideline on the Internet]. Diabetes care. 2010. 2010 Jan [cited 2010 Jan 26]; 33 suppl 1:S11-61. Available from: http://care.diabetesjournals.org/content/33/Supplement_1/S11.full.pdf+html

FDA Updates, Health Reform Legislation, Outgoing Member of the DUR Commission

FDA Update

- Desipramine labeling has been updated with new safety information. The updated label states "extreme caution should be used when this drug is given to patients who have a family history of sudden death, cardiac dysrhythmias, and cardiac conduction disturbances; and that seizures precede cardiac dysrhythmias and death in some patients." The label also warns that rates of death associate with desipramine overdose are higher that those of other tricyclic antidepressants.

- Due to reports of dispensing errors due to confusion with the drugs Casodex® (bicalutamine) and Kadian® (morphine sulfate), the FDA has approved the name change for the drug Kapidex™ (dexlansoprazole). Effective April 2010, Kapidex™ will be marketed under the new name Dexilant™.

- The FDA notified healthcare professionals regarding changes to the label for all diclofenac sodium containing products (including Voltaren gel®). New warnings and precautions are being added about the potential for elevation in liver function tests during treatment with diclofenac sodium. Cases of severe hepatic reactions, including liver necrosis, jaundice, hepatitis, and liver failure resulting in fatalities or liver transplantation have been reported. Transaminases should be monitored within 4 to 8 weeks after beginning treatment with diclofenac, based on postmarketing experiences and clinical trial data.

- The FDA issued a warning about a higher risk of myopathy in patients taking 80mg Zocor® (simvastatin) compared to patients taking lower doses of simvastatin–and possibly other statins.

Health Reform Legislation

- The President recently signed into law the Healthcare Reform bill which will allow for coverage expansion of uninsured persons beginning in 2014.

- Medicaid will be expanded to 133% of poverty level increasing Medicaid coverage by 16 million. Overall, the bill is expected to increase the number of Americans with insurance coverage to 92% of the population (95% excluding illegal immigrants) and increase the number of insured people by 32 million by 2019.

- The cost of Medicaid expansion will be fully funded by the federal government through 2016 at which time the federal matching rate will be decreased to 90% by 2020 for newly covered members.

Outgoing Member of the DUR Commission

Bruce Alexander, R.Ph., Pharm.D., has completed an eight year term of service with the Iowa Drug Utilization Review Commission. The Commission and the Department of Human Services wish to thank Dr. Alexander for his many years of service to the Commission and the members of Iowa Medicaid.

DUR Activities

- The Commission finalized the Smoking Cessation report to the Department. A link to the report can be found on the Iowa Medicaid Drug Utilization Review website at iadur.org.
- The Commission mailed out the Quarterly Narcotic Utilization Report to Prescribers in February 2010. A total of 1,976 letters were mailed. DUR staff continues to receive phone calls from providers stating they do not have record of treating a listed member. The most common reason for this is incorrect information entered by the pharmacy. Prescribers need to contact the listed dispensing pharmacy to correct the information as Iowa Medicaid does not have the ability correct this. Prescribers also need to keep their information current with Iowa Medicaid by contacting Prescriber Services any time their information changes. Provider Services can be reached at 1-800-338-7909 or 515-256-4609.

Medicaid Statistics for Prescription Claims

from January 1, 2010 to March 31, 2010

Number of claims paid: 1,065,956

Total dollars paid: $63,820,590.81

Percent controlled substances: 18.59%

Average amount paid per claim: $59.87

Average amount paid per claim, brand: $204.78

Average Amount paid per claim, generic: $11.95

Top Drugs by Number of Prescriptions*	Top Drugs by Dollars Spent (Pre-Rebate)	Top Therapeutic Class by Dollars Spent (Pre-Rebate)
ProAir HFA $43.76/RX	Synagis 100mg/ml $1.8 million $2,104.44/RX	Antipsychotics – Atypicals $10.8 million
Hydrocodone/APAP 5-500 $4.68/RX	Concerta 36mg $980,930 $194.74/RX	Stimulants – Amphetamines – Long Acting $4.1 million
Lexapro 20mg $87.14/RX	*Abilify* 5mg $956,985 $411.25/RX	Anticonvulsants $3.8 million
Cheratussin AC $5.96/RX	*Adderall* XR 20mg $923,136 $254.17/RX	Antidepressants – Selected SSRI's $3.7 million