Team Name: Regional Pharmacy & Therapeutics Committee Team Lead: Regional Director - Pharmacy Approved by: VP - Medical Services	Reference Number: CLI.6010.PL.007 Program Area: Pharmacy and Therapeutics Policy Section: General
Issue Date: March 23 2017 Review Date: Revision Date:	Subject: Acetylcholinesterase Inhibitors

POLICY SUBJECT:
Acetylcholinesterase Inhibitors

BOARD POLICY REFERENCE:
Executive Limitation (EL-2) Treatment of Clients

POLICY:
Acetylcholinesterase inhibitors may provide symptomatic treatment in some patients with mild to moderate Alzheimer's Disease. This policy seeks to guide appropriate use of these agents for the residents and patients of Southern Health-Santé Sud Personal Care Homes and Hospitals. This will include trial evaluations and discontinuations of acetylcholinesterase inhibitors to monitor efficacy.

PROCEDURE:

1. *Initiation of Therapy:*
   - 1.1. The patient must have a confirmed diagnosis of Alzheimer's Disease (DSM-IV) or Lewy Body Disease and a Mini-Mental State Examination (MMSE) score between 10 and 26.
   - 1.2. The initial assessment must also include normal values for routine blood tests (CBD, TSH, Vitamin B12, Glucose).
   - 1.3. The Exception Drug Status (EDS) Cholinesterase Inhibitor Request Form should be completed and faxed to Manitoba Health in patients who are returning to the community.
   - 1.4. Patients will be provided with a 3-month trial with documentation of clinical benefit and stabilization of MMSE required for ongoing use.
   - 1.5. Patients should not be taking anticholinergic medications as per Table 1
2. *Continuation of Therapy and Coverage of Acetylcholinesterase Inhibitors:*
   - 2.1. Patients showing benefit should be reviewed every 6 months.
   - 2.2. Patients must show an improvement or stabilization of symptoms and have a MMSE score greater than 10 in order to continue to receive coverage.
   - 2.3. Patients with a consistent greater or equal to 3 point drop in MMSE with clinical deterioration between 6 month reviews should have therapy discontinued (i.e. if the MMSE drops by greater than or equal to 3 points on any evaluation, the test should be re-administered within 2 weeks to confirm the drop).
   - 2.4. Patients that are intolerant of one acetylcholinesterase inhibitors may switch to another agent.
   - 2.5. Patients that have failed one agent will not be considered for coverage for other acetylcholinesterase inhibitors.
   - 2.6. Patients should not be taking concurrent anticholinergic medications as per Table 1.

3. *Trial Discontinuation for PCH Residents:*
   3.1. All PCH residents and their families should be informed that medications will be reassess after adminission to PCH.
   3.2. During first 3 months after admission acetylcholinesterase inhibitors may be maintained and baseline MMSE scores obtained. During this period, clear documentation of the patient's mental status should be recorded as a baseline. This documentation should include patient's ability to conduct activities of daily living such as feeding and ambulation. As well, documentation of cognitive function including memory, communication skills and concentration. Finally, documentation of the patient's behavioural tendencies including patterns in the frequency, duration, potential triggers and consequences.
   3.3. All residents receiving acetylcholinesterase inhibitors will undergo discontinuation after this 3-month period to determine significant benefit.
   3.4. Dosage will be reduced by 50% (unless on lowest dose) for 1 month and then discontinued.
   3.5. Observation of behavior and repeat MMSE 4 weeks after discontinuation.
   3.6. Clinically relevant deterioration in behavior or mental status (greater or equal to 3 point drop in MMSE) during dosage reduction and discontinuation warrants re-starting the acetylcholinesterase inhibitor.
   3.7. Patient's that are restarted during the Trial Discontinuation should be monitored as per the Continuation of Therapy and Coverage of Acetylcholinesterase Inhibitors procedure above.
4. *Alternate Arrangements and Appeals:*
   4.1. Residents who do not qualify for acetylcholinesterase therapy (lack of clinical benefit, MMSE criteria) but they or their families wish to continue the treatment may do so with a prescriber's order and billing drug cost to the family.
   4.2. Prescriber's who care for residents that do not qualify for acetylcholinesterase therapy may apply in writing to the Chair of the Pharmay and Therapeutics Committee. The information provided should include history of acetylcholinesterase use, dosage, MMSE scores and descriptive evidence of clinical changes, functional status or behavious scores. These applications will be referred to a specialist (geriatrician/psychiatrist) for consideration. For patients already established on acetylcholinesterasetherapy, the medication will continue to be provided until a decision on the appeal has been received. Approval will require the development of an explicit monitoring plan to evaluate efficacy and a plan for discontinuation if clinically significant efficacy is not evident.

IMPORTANT POINTS TO CONSIDER:

- Both the family and prescribers should be aware of the significant limitations in efficacy of acetylcholinesterase inhibitors. Many patients may not respond to acetylcholinesterase treatment. Even in patients that show significant response most patients will experience a progression of the disease that will at some point make further use of acetylcholinesterase inhibitors inappropriate. If appropriate, patients and their family should be provided the Acetylcholinesterase Patient Brochure.
- Under this program patients not showing an improvement or stabilization of symptoms and an MMSE of greater than 10 are seen to not be benefiting from the medication and will no longer receive coverage for the medication. When this occurs the acetylcholinesterase inhibitor should be discontinued.

SUPPORTING DOCUMENTS:

Acetylcholinesterase Patient Brochure CLI.6010.PL.007.SD.01

REFERENCES:

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TABLE 1: AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation	References
Anticholinergics (excludes TCAs)					
First-generation antihistamines (as single agent or as part of combination products) Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Dexchlorpheniramine Diphenhydramine (oral) Doxylamine Hydroxyzine Promethazine Triprolidine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/toxicity. Use of diphenhydramine in special situations such as acute treatment of severe allergic reaction may be appropriate.	Avoid	Hydroxyzine and promethazine: high; All others: moderate	Strong	Agostini 2001 Boustani 2007 Guaiana 2010 Han 2001 Rudolph 2008
Antiparkinson agents Benztropine (oral) Trihexyphenidyl	Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease.	Avoid	Moderate	Strong	Rudolph 2008