Background

“Our mission is to cause patients no harm while managing their health with medication.”

Drug induced dementia may be the cause of cognitive impairment in about 12% of patients with suspected dementia. The relative odds of drug-induced dementia increases as the number of medications rises. Drugs may impair cognition indirectly by metabolic effects, such as hypoglycaemia, by alterations of immunological factors within the CNS and by actions that interfere with synaptic transmission. Classes of drugs most often associated include benzodiazepines, antihypertensives and anticholinergic agents.

Delirium is not uncommon in patients with dementia and should not be ruled out when a patient with dementia suddenly develops a change in mental status. Delirium, which is a syndrome of changes in attention perception (vision & hearing) and thinking, is more commonly seen in a hospital setting or during an acute illness. It usually starts abruptly and has a fluctuating course. The most common cause is acute medical illness e.g. infection or medication. Polypharmacy may predispose patients to develop drug-induced delirium.

Approximately 20%-30% of patients with Parkinson’s disease have a concomitant dementia and they are especially prone to the development of drug-induced cognitive impairment. Early clues to worsening of cognitive function may include abnormal dreaming and sleep disturbances. If a patient develops drug-induced cognitive impairment while on multiple anti-Parkinson’s medication, it may be beneficial to slowly withdraw the anticholinergics, selegiline and amantadine before removing the other drugs.

Patients with bipolar affective disorder taking lithium are also more likely to experience cognitive impairment. Lithium toxicity is potentiated by drugs such as thiazide diuretics, ACE inhibitors and NSAIDs which interact with lithium to produce higher lithium levels.

Evidence has shown that patients with Alzheimer’s disease being treated with acetylcholinesterase (AchE) inhibitors have greater decline in their mental status when tested after taking concurrent anticholinergic drugs for 2 years. AchE inhibitors act by increasing or maintaining levels of acetylcholine within the brain, through inhibiting the enzyme acetylcholinesterase. The effect of AchE inhibitors is antagonised by drugs with anticholinergic properties (see Appendix 1 for abbreviated list) therefore reducing their effect.
**Reason for review**
Elderly patients and those with Parkinson’s disease are at greater risk of side effects from medication and in particular their impact on mental state. Taking a thorough drug history should be one of the first actions when assessing an older patient with changes in cognitive function. Note that OTC medication such as sedative antihistamines and herbal products e.g. St John’s Wort can also be associated with confusion.

Older people are more susceptible to drug-induced delirium and dementia because:

1. The body’s ability to clear drugs decreases with age, often because of normal age-related decrease in kidney and liver function. This results in greater accumulation of drugs in the body.
2. Older patients are often prescribed multiple drugs at the same time. Due to complicated interactions between different drugs, side effects can become more prominent.
3. Some research suggests that neurotransmitters become naturally imbalanced as people age, increasing the brain’s sensitivity to drugs that have activity in the CNS.

The avoidance of drugs with anticholinergic properties (e.g. urinary frequency drugs, sedating antihistamines, benzodiazepines, TCAs) minimises the risk of cognitive impairment or other central nervous system side effects in patients with Alzheimer’s disease. Although discontinuation of anticholinergic drugs is encouraged in this patient group, rapid withdrawal of these drugs may result in cholinergic rebound. Secondly, doses should be adjusted based on age (frailty), renal and hepatic function. Wherever possible, every attempt should be made to avoid high-risk medications such as sedative-hypnotics and drugs with anticholinergic effects, as well as other drugs that may readily cross the blood-brain barrier.

**Inclusion Criteria**
- Patients on the dementia register including those on AchE inhibitors
- Patients with Parkinson’s disease on multiple medications including ones with anticholinergic side effects
- ***Patients on a combination of AchE inhibitors and anticholinergic drugs should be brought to urgent attention of GP***

**Exclusion criteria**
- Palliative care
- Any individual patient exclusions deemed necessary by the GP(s)

**Preparation and Planning**
Implementation of the audit in selected GP practices by the Prescribing Support Team is as follows
- Protocol to be discussed with all GPs in the practice to ensure that agreement to proceed is reached
- Computer search of all the patients according to the inclusion criteria
- A list to be produced of patients meeting the above inclusion criteria

List of eligible patients to be reviewed by GP and invited in (with carer when required) to discuss the changes proposed to their medication in relation to cognitive function

**Action**
Letters to be sent to eligible patients inviting them to attend the surgery for review of their medication
### List of most common drugs associated with anticholinergic side effects

The higher the number, the higher the ACB*. Please note this list is not exhaustive.

#### ACB = 3
- amitriptyline
- atropine
- chlorpromazine
- chlorpheniramine
- clemastine
- clozapine
- dicycloverine
- glycopyrronium
- hydroxyzine
- oxybutynin

#### ACB = 2
- amantadine
- baclofen
- carbamazepine
- cetirizine
- cimetidine
- doxepin
- diphenhydramine
- darifenacin
- flavoxate
- hyoscine
- imipramine
- loperamide
- loratadine
- nortriptyline
- orphenadrine
- pethidine
- procyclidine
- promazine
- promethazine
- prochlorperazine
- propantheline
- solifenacin
- tropium
- trimipramine
- tolterodine
- solifenacin
- scopalamine

#### ACB = 1
- alverine
- atenolol
- beclometasone
- chlorthalidone
- codeine
- captopril
- chlordiazepoxide
- colchicine
- diazepam
- digoxin
- dipyridamole
- furosemide
- fentanyl
- hydralazine
- haloperidol
- morphine
- mirtazapine
- metoprolol
- nifedipine
- olanzapine
- paroxetine
- quetiapine
- ranitidine
- trazodone
- triamterene
- theophylline
- warfarin

*ACB – acetylcholine burden