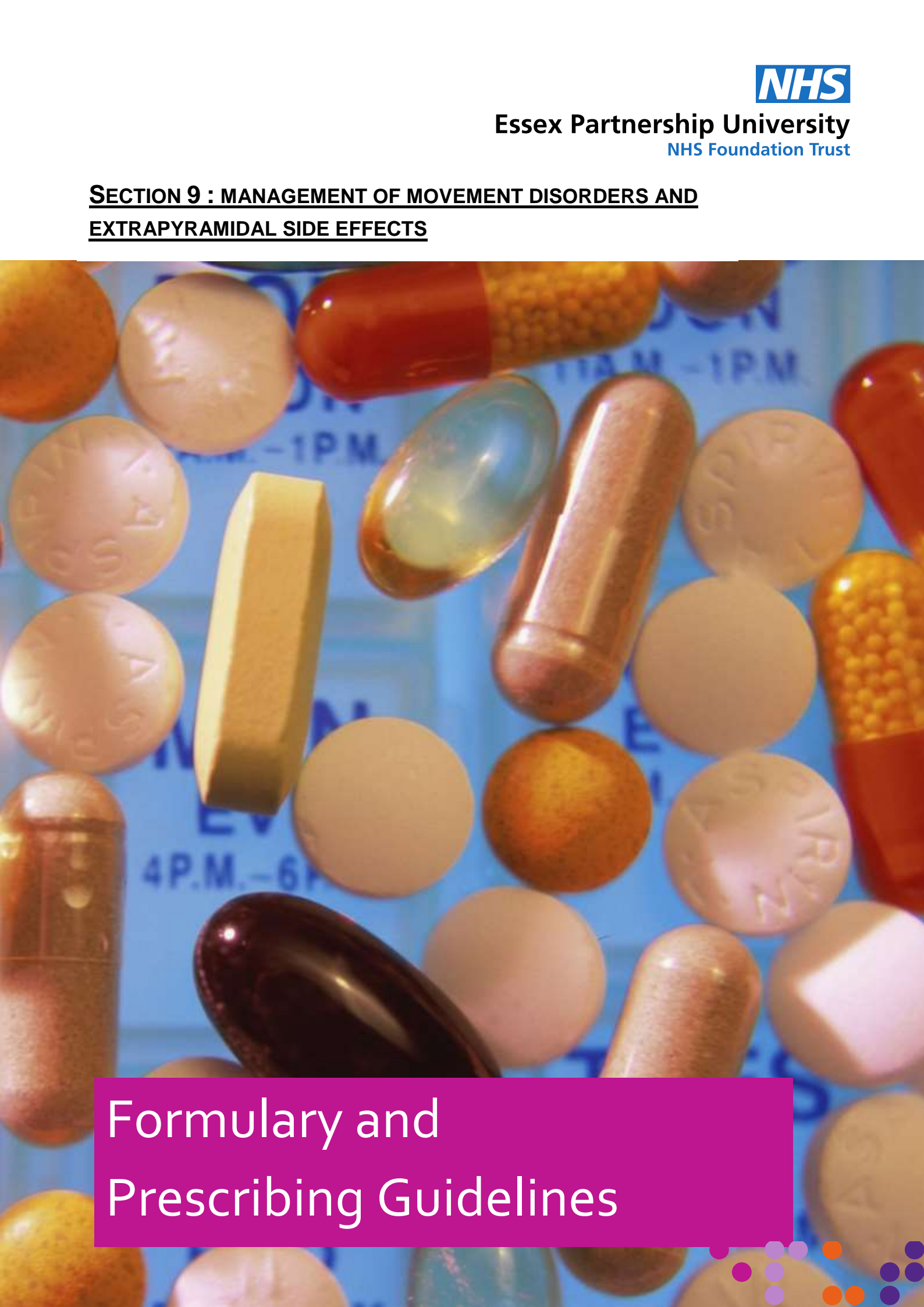


**SECTION 9 : MANAGEMENT OF MOVEMENT DISORDERS AND
EXTRAPYRAMIDAL SIDE EFFECTS**

A close-up photograph of various pills and capsules scattered on a light blue surface. The pills are in various shapes, sizes, and colors, including white, yellow, orange, red, and black. Some have markings like 'ESVA' or 'BRN'. The background is slightly blurred, showing some text like '11AM-1PM' and '4PM-6PM'.

Formulary and
Prescribing Guidelines

A decorative graphic in the bottom right corner consisting of a cluster of colored dots in shades of purple, blue, and orange.

9.1 Introduction

Movement disorders and extrapyramidal side effects can manifest in the following symptoms:

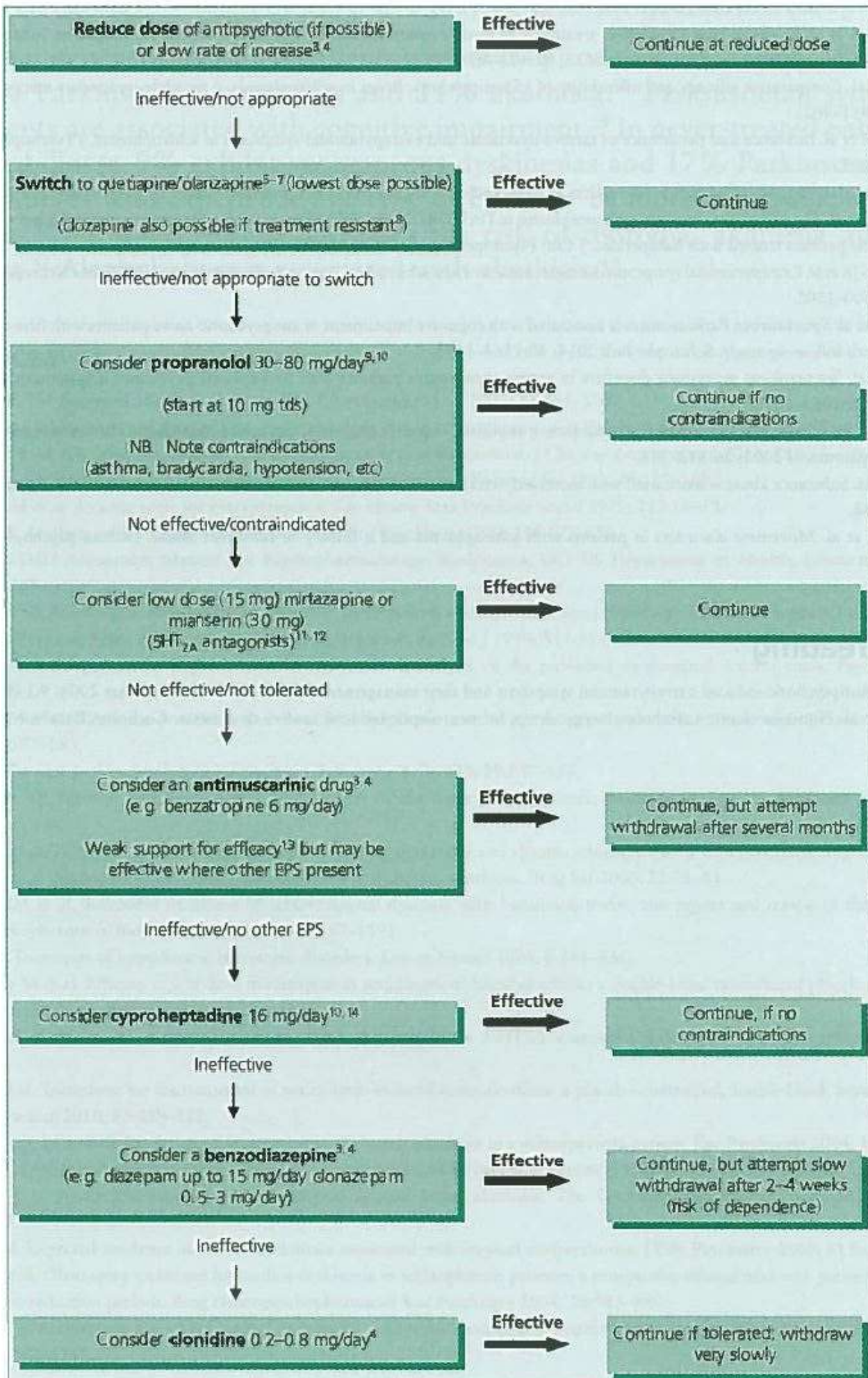
- Akathisia (restlessness), which characteristically occurs after large initial doses and may resemble an exacerbation of the condition being treated.
- Blepharospasm is a sustained, forced, involuntary closing of the eyelids often a symptom of tardive dystonia and is often caused by antipsychotic treatment.
- Bruxism (teeth grinding)
- Dysphagia (difficulty in swallowing or painful swallowing)
- Dystonia (abnormal face and body movements, including oculogyric crisis) and dyskinesia, which occur more commonly in children and young adults and may appear after only a few doses
- Parkinsonian symptoms (including tremor), which may occur more commonly in adults or older adults and may appear gradually
- Tardive Dyskinesia (rhythmic, involuntary movements of tongue, face and jaw), which usually develops on long-term therapy or with high dosage, but it may develop on short-term treatment with low doses – short lived tardive dyskinesia may occur after withdrawal of the drug. Tardive Dyskinesia is not improved by antimuscarinic drugs and may be made worse

9.1 Treatment options – see current BNF for doses

Outlined below is a summary of common options for the treatment of movement disorders. For other alternative treatments contact the pharmacy department for advice.

Akathisia (including restless leg syndrome) - If caused by antidepressants reduce the dose or switch an alternative antidepressant. Propranolol may be helpful.

If caused by antipsychotics reducing the dose or switching to an alternative drug may be helpful. The use of adjunctive therapies such as anticholinergic, antimuscarinic drugs e.g. procyclidine, trihexyphenidyl may be of some use, alternatively benzodiazepines e.g. clonazepam or beta blockers e.g. propranolol can be prescribed. The flow chart below outlines further options³. The FDA has warned of a serious risk of death when benzodiazepines are used in combination with Opioid analgesic or cough preparations.⁵



Blepharospasm - Switch antipsychotic to Clozapine or Quetiapine. ECT may be helpful.

Bruxism - If caused by antidepressants a dose reduction usually leads to resolution, but the symptoms can take several months to subside. Switching to another drug in the same class may help. There is some evidence that Buspirone 40mg/day over 4 weeks can be effective as can Gabapentin if the condition is caused by venlafaxine.

If caused by antipsychotics a reduction in the dose is usually successful. Alternatively switch to low dose clozapine (unlicensed). Lamotrigine and propranolol have also been shown to be helpful.

Dysphagia - May be caused by treatment with antipsychotics. A rapid response is usually seen to the discontinuation of the drug. Benzodiazepines e.g. clonazepam or anticholinergics e.g. trihexyphenidyl or benztropine may be helpful, although if used regularly anticholinergics may be a causative or exacerbating factor.

Dystonia - If caused by antidepressants switching drugs is the main strategy. Low dose aripiprazole can be used for orofacial and buccal dystonias from SSRIs.

Antipsychotic induced acute dystonias can be improved by switching to an alternative antipsychotic. Anticholinergics e.g. procyclidine are the first line treatment. Diphenhydramine has also been shown to produce a rapid reversal of dystonias such as oculogyric crisis.

Parkinsonian Symptoms - If caused by antidepressants switching to an alternative is the first option. Alternatively diazepam or propranolol can be prescribed. If caused by antipsychotics a lower dose may be helpful if mental state allows. Alternatively switch to quetiapine, olanzapine or aripiprazole. Anticholinergics e.g. procyclidine or trihexyphenidyl can be tried.

Tardive Dyskinesia - Usually caused by antipsychotics. Switching to an alternative second generation antipsychotic is first line. Adjunctive therapies e.g. amantadine and buspirone can be tried, although there is limited evidence of efficacy.

Recommended Anticholinergic Drugs.

Drug	Formulations ¹	Comments ²
Procyclidine	Injection 5mg/mL; Tabs 5 mg; Syrup 5mg/5mL.	Procyclidine is indicated for the control of extrapyramidal symptoms induced by neuroleptic drugs including pseudo-parkinsonism, acute dystonic reactions and akathisia.- 1st line Caution: abuse potential; risk of diversion After a period of 3 to 4 months of therapy, procyclidine should be withdrawn. If neuroleptic EPSE reoccurs, procyclidine should be reintroduced to avoid debilitating EPSE. Cessation of treatment periodically is recommended even in patients who appear to require the drug for longer periods.
Trihexyphenidyl (Benzhexol)	Tabs 2mg 5mg; Syrup 5mg/5mL.	Licensed for parkinsonism and drug induced extrapyramidal syndrome.
Hyoscine Hydrobromide	Tabs 300mcg	Unlicensed indication for hypersalivation associated with clozapine therapy

Orphenadrine is non-formulary due to the risk of toxicity.

Side effects of anticholinergics include constipation, dry mouth, nausea, vomiting, tachycardia, dizziness, confusion, euphoria, hallucinations, impaired memory, anxiety, restlessness, urinary retention, blurred vision, and rash. Closed angle glaucoma may also occur very rarely. Performance of skilled tasks (e.g. driving) may be impaired.

Anticholinergics should be used with extreme caution in patients predisposed to angle-closure glaucoma or those with urinary symptoms in association with prostatic hypertrophy. They should be avoided in patients with myasthenia gravis and gastrointestinal obstruction. They should also be used with caution in cardiovascular disease and pyrexia. Anticholinergics should not be routinely (if at all) used in older adults. This group is especially vulnerable to confusion, impairment of cognitive function and memory, disorientation and hallucinations caused by anticholinergics. There have been reports of precipitation of psychotic episodes in patients taking anticholinergics for extrapyramidal side effects of antipsychotics so prescribers should bear this in mind if any new symptoms arise. Anticholinergics can exacerbate the symptoms of tardive dyskinesia (TD) in patients taking antipsychotics, and whilst they are not the cause of TD, they can reduce the threshold at which this movement disorder occurs in predisposed patients.

All anticholinergics should be gradually withdrawn and not abruptly terminated as rebound parkinsonian symptoms may occur. Attempts at gradual withdrawal should be made after three months of therapy if prescribed for extrapyramidal symptoms of antipsychotics, and re-commenced only if symptoms reoccur. All the anticholinergics have the potential to be abused and clinical need should be reviewed regularly.

Drug interactions can be common with anticholinergics (see latest BNF). A special warning has been highlighted with the concurrent use of anticholinergics and anti-arrhythmics (amiodarone, disopyramide or flecanide) and cardio-selective beta blockers (sotolol).

In a 2002 Cochrane review of the efficacy of anticholinergics (in Parkinson's disease), the authors concluded that these agents are more effective than placebo in improving motor function (in Parkinson's Disease) but that neuropsychiatric and cognitive adverse effects occurred more frequently (relative to placebo) and were a common reason for withdrawal. The authors cited that the data did not support a differential effect of anticholinergics on individual parkinsonian features such as tremor, nor was there sufficient evidence to allow comparisons with respect to efficacy or tolerability between the individual anticholinergic medicines (orphenadrine, benzhexol, bengtropine).

References

1. BNF on-line edition, October 2017
2. Summary of Product Characteristics for Individual Drugs
<http://www.medicines.org.uk/EMC/> (Accessed October 2017)
3. South London & Maudsley NHS Foundation Trust Prescribing Guidelines 12th edition, Wiley Blackwell, 2015
4. Psychotropic Drug Directory 2016, Bazire S. Lloyd-Reinhold Publications Ltd (15 April 2016)
5. <http://www.fda.gov/Drugs/DrugSafety/default.htm> Accessed September 2016