PAN MERSEY APC

NHS
Pan Mersey
Area Prescribing Committee

ATYPICAL ANTIPSYCHOTICS

INFORMATION TO SUPPORT PRIMARY CARE PRESCRIBING AND DISCHARGE FROM NORTH WEST BOROUGHS SPECIALIST SERVICES

1: BACKGROUND

Atypical antipsychotics are classed as Amber Initiated drugs by the Pan Mersey Area Prescribing Committee, allowing:

- The transfer of prescribing from secondary to primary care after successful initiation and stabilisation
- Appropriate patients to be discharged from secondary care services when both secondary and primary care clinicians agree it is appropriate to do so.

This document aims to provide information to support GPs in these activities.

This document covers the use of atypical antipsychotics (except clozapine) for the following indications:

- Schizophrenia
- Bipolar illness
- Schizoaffective illness
- Adjunctive treatment in major depressive disorder (where licensed)
- Psychotic symptoms such as hallucinations, thought disorder, paranoia, delusions, conceptual disorganisation, grandiosity and psychomotor agitation in those who do not have a diagnosis of schizophrenia or bipolar illness.

Key Points

1. This document supports primary care **prescribing** of oral atypical antipsychotics when:
    - The patient's condition is stable and under review by the specialist team.
    - The prescribed antipsychotic medication is effective and tolerated.
    - The patient is content to stay on the drug and dose.
    - Compliance is established to the satisfaction of the specialist team

Note: The responsibility for monitoring the patient remains with secondary care

2. This document supports the **discharge** of patients from secondary care whilst the patient is taking an oral atypical antipsychotic when:
    - The specialist team has determined that the patient's condition is stable and relapse is not expected.
    - The specialist team has determined that the patient's condition is stable on the current medication regime
    - Drug treatment is effective and tolerated.
    - Compliance is established to the satisfaction of the specialist team
    - The patient is content to stay on the drug and dose.

3. Any patient who is referred and has been previously discharged under this Amber Initiated process will always be accepted back into services via the normal referral pathway.

2: PRESCRIBING

2.1 Who will diagnose and decide who is suitable for which drug?

- Specialists will diagnose and assess suitability and safety, of atypical antipsychotic drug treatment for patients.
- Specialists will counsel and inform patients of their diagnosis and treatment options.
- Specialists will follow up the patients until the patient is discharged

2.2 Who will amend the dose regime?

The patient will be deemed to be on the most effective tolerated dose of medication when the primary care request to continue prescribing is made.

The specialist is responsible for all dose alterations whilst the patient is under the care of specialist services.

Post discharge, the GP may seek advice from the specialist service if they consider a dose alteration is appropriate or re-refer the patient back to the specialist service.

2.3 When is it appropriate to request primary care prescribing?

Once the most effective and tolerated dose of medication has been established and compliance is assured.

2.4 Guidance for GPs who take on prescribing responsibilities

- Provide regular prescriptions for atypical antipsychotics.
- Be aware of side effects and common drug interactions as documented in this guideline.

2.5 Contact Specialist Services if:

- Any concerning adverse-effects arise
- If a dose change is being considered
- Any advice pertaining to treatment is required

2.6 Who will follow up and monitor patients?

Specialist services will follow up and monitor patients prescribed atypical antipsychotic medication unless the patient has been discharged from Specialist Services.

Patients will only be discharged from Specialist Services should they meet the suitability criteria described in this document and where both secondary and primary care agree it is appropriate to do so.

Once the patient has been discharged to primary care the GP has responsibility for follow up and monitoring (details in section 5).

3: DISCHARGE

3.1 When will the patient be suitable for discharge?

Patients can only be discharged from Specialist Services should they meet the suitability criteria described in Key Point 2 on page one of this document and where both secondary and primary care agree it is appropriate to do so.

Patients on quetiapine as adjunctive treatment in major depressive disorder can be discharged as soon as treatment is deemed effective and tolerated and the dose has been stabilised.

3.2 Guidance for GPs post discharge

Tolerability may change over time consequent to the emergence of medical co-morbidities, potential drug interaction and alcohol and drug misuse; therefore GPs are expected to provide regular health checks and provision of advice about lifestyle.

3.3 Contact Specialist Services if:

- Any concerning adverse-effects arise
- If a dose change is being considered
- Any advice pertaining to treatment is required

In these situations GPs are encouraged to contact services for advice without re-referral in the first instance.

3.4 Re-refer to Specialist Services if:

- There is a deterioration/concern regarding the patient's mental health - note the Specialist Service can see the patient the same day in an urgent acute situation
- A patient is expressing a wish to stop the atypical antipsychotic medication for a psychotic illness (see quetiapine use in depression above)
- There are concerns regarding treatment compliance
- A patient's cardiac health changes - appropriateness of prescription will need to be discussed and consideration given for referral to cardiology.
- Any other concerning physical health problems arise which may relate to, or impact on, treatment
- There are any concerning abnormal physical or laboratory results that may relate to atypical antipsychotic drug treatment
- The GP believes it is appropriate to do so

If there is a need to re-refer; patients who have been previously discharged will always be accepted back into Specialist Services via the normal referral pathway.

3.5 What is the advice regarding 'drug holidays'?

'Drug holidays' are not advised

3.6 When should the drug be stopped?

There is a high risk of relapse if the drug is stopped. If a patient is expressing a wish to stop medication for a psychotic illness they should be referred back to specialist services.

4: MONITORING

Specialist Services will be responsible for the monitoring of physical health relevant to the drug at baseline and through the stabilisation period until discharge

After discharge the patient's GP will be responsible for the ongoing monitoring of physical health relevant to the drug as indicated in the table below.

	Annual check up	Drug specific interim monitoring requirements ANTIPSYCHOTICS
Fasting BM, or HbA1c	✓	**Olanzapine** requires 6 monthly monitoring
Lipids	✓	
FBC	✓	
LFT's	✓	
U+E's	✓	
TFT's	✓	In those with bipolar disorder
Prolactin		**I**f signs of hyperprolactinaemia Discuss raised levels with biochemistry
ECG+CVD assessment	✓	
BP + Pulse	✓	
Weight	✓	

5: GENERAL INFORMATION

5.1 Drug Selection

Unfortunately it is not possible to predict the response to any particular antipsychotic for a given individual and therefore drug selection is based on the possible impact of common adverse effects, co-morbidities, co-prescribed medication and response to any previous treatments.

As a general rule atypical antipsychotics, also known as second generation antipsychotics, are less likely to cause extrapyramidal side effects than typical/first generation antipsychotics.

Atypical antipsychotics licensed in the UK and listed in the Pan-Mersey formulary include: amisulpride, aripiprazole, clozapine, lurasidone, olanzapine, paliperidone, quetiapine and risperidone.

Clozapine requires stringent and frequent monitoring; for this reason it has a hospital only status in the Pan-Mersey formulary and is therefore excluded from the Amber Initiated process.

5.2 Mode of Action

Antipsychotics are thought to work by blocking/inhibiting dopamine and serotonin receptor subtypes within the CNS. All antipsychotics differ in their receptor profile activity which results in large inter-patient variation in terms of efficacy and tolerability.

5.3 Dosage

Source BNF edition 73, Electronic Medicine Compendium [accessed Aug 2017)

Atypical antipsychotics are mainly used to treat symptoms of psychosis irrespective of diagnosis; however, quetiapine is also licensed as an adjunct in major depression

Drug	Posology - Adults
Amisulpride	**Positive symptoms** Usual treatment dose: 400-1200 mg/d Max dose: 1200 mg/d **Negative symptoms** Usual treatment dose: 50 – 300 mg/d
Aripiprazole	Usual treatment dose: 15-30 mg/d Max dose: 30 mg/d
Lurasidone	Usual treatment dose: 37 -148 mg/d Max dose 148mg/d
Olanzapine	Usual treatment dose: 5-20 mg/d Max dose 20 mg/d
Paliperidone	Usual treatment dose: 3-12 mg/d Max dose 12 mg/d
Quetiapine	**Schizophrenia** Usual treatment dose: 300-450 mg/d Max dose: 750 mg/d **Mania** Usual treatment dose: 400-800 mg/d Max dose: 800 mg/d **Depression in bipolar disorder** Usual treatment dose: 300 mg/d Max dose: 600 mg/d **Bipolar prevention** Usual treatment dose: 300-800 mg/d Max dose: 800 mg/d

Drug	Posology - Adults
Quetiapine XL **Any request for a modified release version should be supported by a statement of clinical need**	**Schizophrenia** Usual treatment dose: 600 mg/d Max dose: 800 mg/d **Mania** Usual treatment dose: 400-800 mg/d Max dose: 800 mg/d **Depression in bipolar disorder** Usual treatment dose: 300 mg/d Max dose: 600 mg/d **Bipolar prevention** Usual treatment dose: 300-800 mg/d **Adjunct in major depression** Usual treatment dose: 150-300 mg/d
Risperidone	**Schizophrenia** Usual treatment dose: 4-6 mg/d Max dose: 16 mg/d **Mania** Usual treatment dose: 1-6 mg/d Max dose: 16 mg/d **Psychosis** Usual treatment dose: 4-6 mg/d Max dose: 16 mg/d

5.4 Common Adverse Effects

Source BNF edition 73, Electronic Medicine Compendium [accessed Aug 2017)
See latest BNF and SPCs for most up to date information

The following are ADRs listed by system organ class that occur at a frequency ≥ 1/100. Each applies to one or more of the atypical antipsychotics listed in this document rather than every drug. The intention is to provide the reader with an overview of adverse effects that are most likely to affect patients.

Note that primary care should only be contacted once 'stability' has been achieved which includes tolerance to the chosen treatment; however, all responsible medics need to be aware of the following in case of an evolving problem/new illness post stabilisation.

Blood and lymphatic system disorders
Decreased haemoglobin, eosinophilia, high uric acid, increased alkaline phosphatase, increased creatinine phosphokinase, leukopenia, neutropenia, oedema, raised lipids

Cardiac disorders
Atrioventricular block, bradycardia, conduction disorder, hypotension, palpitations, QT prolongation, tachycardia

Endocrine disorders
Hyperprolactinaemia, decreases in total T4, free T4, total T3; increases in TSH hyperglycaemia, diabetes mellitus,

Eye disorders
Blurred vision

Gastrointestinal disorders
Abdominal discomfort/pain, constipation, diarrhoea, dry mouth, dyspepsia, hypersalivation, nausea, toothache, vomiting

Hepatobiliary disorders
Raised hepatic enzymes

Infections and infestations
Bronchitis, influenza, sinusitis, upper respiratory tract infection, urinary tract infection

Metabolism and nutrition disorders
Appetite/weight - increase/decrease,
Elevations in total cholesterol (predominantly LDL cholesterol), serum triglyceride levels and blood glucose
Decreases in HDL cholesterol

Musculoskeletal and connective tissue disorders
Musculoskeletal pain, back pain, arthralgia

Nervous system disorders
Akathisia, dizziness, dysarthria, dyskinesia, dystonia, extrapyramidal symptoms, headache, Irritability, Parkinsonism, pyrexia, restlessness, sedation, somnolence, tremor

Psychiatric disorders
Abnormal dreams, agitation, anxiety, depression, insomnia, mania, nightmares somnolence, suicidal ideation/behaviour

Renal and urinary disorders
Glucosuria

Reproductive system and breast disorders
Amenorrhoea, breast pain, erectile dysfunction, galactorrhoea, gynaecomastia, orgasmic dysfunction, sexual dysfunction

Respiratory, thoracic and mediastinal disorders
Cough, dyspnoea, nasal congestion, pharyngolaryngeal pain

Skin and subcutaneous tissue disorders
Pruritus, rash

Vascular disorders
Orthostatic hypotension, hypertension

General disorders - Asthenia, fatigue, peripheral oedema, pyrexia, withdrawal symptoms

Medical Emergency – Neuroleptic Malignant Syndrome (NMS)
NMS is a rare, potentially fatal symptom complex associated with antipsychotic medicinal products. Clinical manifestations of NMS include confusion, hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

If a patient develops signs and symptoms indicative of NMS, or presents with unexplained high fever without additional clinical manifestations of NMS, all antipsychotic substances must be discontinued and the patient referred to A&E immediately for supportive therapy.

5.5 Cautions

Source BNF edition 73, Electronic Medicine Compendium [accessed Aug 2017)
See latest BNF and SPCs for most up to date information

Note that primary care will only be contacted once 'stability' has been achieved which includes tolerance to the chosen treatment; however, all responsible medics need to be aware of the following in case of an evolving problem/new illness post stabilisation.

The following 'cautions' are listed by system organ class. Each applies to one or more of the atypical antipsychotics listed in this document rather than every drug. The intention is to provide the reader with an overview.

Blood and lymphatic system disorders
Agranulocytosis, leukopenia, neutropenia

Cardiac disorders
Cardiovascular disease, QT prolongation (incl family history), orthostatic /postural hypotension, syncope

Endocrine disorders
Benign pituitary tumour, diabetes mellitus (including risk factors), hyperglycaemia, Hyperprolactinaemia

Gastrointestinal disorders
Untreated constipation, dysphagia, paralytic ileus and related conditions, potential for gastrointestinal obstruction

Hepatobiliary disorders
Hepatic impairment

Nervous system disorders
Parkinson's disease, seizure history

Psychiatric disorders
ADHD, dementia, pathological gambling, suicidal ideation/behaviour, patients with schizoaffective disorder

Renal disorders
Renal impairment

Reproductive system and breast disorders
Galactorrhoea, gynaecomastia, prostatic hypertrophy

Vascular disorders
Stroke, venous thromboembolism risk

Miscellaneous
Acute withdrawal, concomitant use of neuroleptics, elderly patients, breast cancer

5.6 Contra-indications

Source BNF edition 73, Electronic Medicine Compendium [accessed Aug 2017)
See latest BNF and SPCs for most up to date information

Note that primary care will only be contacted once 'stability' has been achieved and the issue of contra-indications will have already being considered; however, all responsible medics need to be aware of the following in case of an evolving problem/new illness post stabilisation.

Drug	Contra-indications	
Amisulpride, Aripiprazole	CNS depression, Comatose states	
Amisulpride, Aripiprazole	Phaeochromocytoma	
Amisulpride	Prolactin-dependent tumours e.g. pituitary gland prolactinomas or breast cancer	
Amisulpride	Lactation	
Lurasidone, Quetiapine	Interactions	Potent CYP3A4 inhibitors/inducers*
Amisulpride		Combination with levodopa
Olanzapine	Patients with known risk of narrow-angle glaucoma.	
All	Hypersensitivity to the active ingredient or to other ingredients of the medicinal product	

*Strong CYP3A4 inhibitors includes: Boceprevir, clarithromycin, cobicistat, grapefruit juice, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole)

*Strong CYP3A4 inducers includes: Carbamazepine, phenobarbital, phenytoin, rifampicin, St John's wort (*Hypericum perforatum*)

5.7 Co-prescribing and interactions

Prescribing software would be expected to identify problematic drug interactions.

Clinicians should also familiarise themselves with the common adverse effects listed above as these may antagonise or enhance the pharmacological actions of co-prescribed medication.
E.g. antipsychotics may lower the seizure threshold and may therefore antagonise the effects of antiepileptic medication.
E.g. antipsychotics can have hypotensive effects and may therefore enhance the effect of antihypertensive medication.

5.8 Related NICE guidance

NICE Psychosis and schizophrenia in adults: prevention and management (CG178)
NICE Bipolar disorder: assessment and management (CG185)
NICE (CG90) supports the use of antipsychotics to combine with/augment a patients existing anti-depressive treatment