Cheshire and Wirral Partnership NHS
NHS Foundation Trust

Document level: Trustwide (TW)
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Policy for prescribing antipsychotic medications in psychotic conditions (excluding Bipolar Disorder)

Lead executive	Medical Director
Author and contact number	Lead Clinical Pharmacist – 01625 663 857

Type of document	Policy
Target audience	All clinical staff
Document purpose	The aim of this policy is to advance cost-effective, evidenced-based prescribing, in line with Clinical Guidance 82, within Cheshire & Wirral Partnership NHS Foundation Trust and beyond.

Document consultation	The Antipsychotic Task & Finish Group, Prescribers within the Trust have been consulted with at various events, such as the Masterclass in Psychopharmacology study day and local Consultant & Managers (CONMAN) meetings, to give their opinion regarding antipsychotic prescribing	
Approving meeting	Medicines Management Group	6-Oct-11
Ratification	Document Quality Group (DQG)	23-Nov-11
Original issue date	Nov-11	
Implementation date	Nov-11	
Review date	Nov-16	

CWP documents to be read in conjunction with	HR6	Trust-wide learning and development requirements including the training needs analysis (TNA)
	MP1	Medicines policy
	MP3	Guidance on the recommended psychotropic agents for use in pregnancy and lactation
	MP6	Introduction of new medicines
	MP9	Policy for the initiation and maintenance of prescribing medicines for “off-label” indications (licensed medicines for unlicensed indications)
	MP10	Rapid tranquilisation policy
	MP18	High Dose Antipsychotic Therapy (HDAT) Guideline

Training requirements	There **are no** specific training requirements for this document.

Financial resource implications	No cost implications with the implementation of this policy but cost savings to be made by following the policy.

Equality Impact Assessment (EIA)

Initial assessment	Yes/No	Comments
Does this document affect one group less or more favourably than another on the basis of:		
• Race	No	
• Ethnic origins (including gypsies and travellers)	No	
• Nationality	No	
• Gender	No	
• Culture	No	

• Religion or belief • Sexual orientation including lesbian, gay and bisexual people • Age • Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No No No No	
Is there any evidence that some groups are affected differently?	No	
If you have identified potential discrimination, are there any exceptions valid, legal and/or justifiable?		
N/A		
Is the impact of the document likely to be negative? • If so can the impact be avoided? • What alternatives are there to achieving the document without the impact? • Can we reduce the impact by taking different action?	No N/A N/A N/A	
Where an adverse or negative impact on equality group(s) has been identified during the initial screening process a full EIA assessment should be conducted.		

If you have identified a potential discriminatory impact of this procedural document, please refer it to the human resource department together with any suggestions as to the action required to avoid / reduce this impact.

For advice in respect of answering the above questions, please contact the human resource department.

Was a full impact assessment required?	No	
What is the level of impact?	Low	

Monitoring compliance with the processes outlined within this document

Is this document linked to the NHS litigation authority (NHSLA) risk management standards assessment?	No NB - The standards in bold above are those standards which are assessed at the level 2 and 3 NHSLA accreditation.

Who is responsible for undertaking the monitoring?	MMG
How are they going to monitor the document?	Audit of clinicians' prescribing of antipsychotic medications in psychotic conditions across CWP and Primary Care. The audit needs to be worked into the MMG audit cycle and the Clinical Consortias'.
What are they going to monitor within the document?	Prescribing adherence within CWP and Primary Care.
Where will the results be reviewed?	MMG
When will this be monitored and how often?	Initial audit within six months of policy implementation and then annually.
If deficiencies are identified how will these be dealt with?	Action plan to be generated from audit results. Disemination of action plan to CSU general managers and clinical directors, and Primary Care representatives for actioning.
Who and where will the findings be communicated to?	MMG
How does learning occur?	Via action plan, and re-audit.
How are the board of directors assured?	MMG annual report.

Document change history

Changes made with rationale and impact on practice
1.

External references

References
1. National Institute of Health and Clinical Excellence Clinical Guideline 82: Schizophrenia 2. The British National Formulary (BNF) 61 March 2011, BMJ Group and Pharmaceutical Press 3. The Maudsley Prescribing Guidelines 10th Edition (2009); Taylor, Patton and Kapur; Informa Healthcare 4. The Psychotropic Drug Directory 2010; Stephen Bazire; HealthComm UK Ltd 5. Duggan L, Brylewski J. Effectiveness of antipsychotic medication in people with intellectual disability and schizophrenia: a systematic review. Journal of Intellectual Disability Research 1999;43:94-104 6. Correll CU. Assessing and maximizing the safety and tolerability of antipsychotics used in the treatment of children and adolescents. Journal of Clinical Psychiatry (2008); 69(4): 26-36 7. Correll CU, Carlson HE. Endocrine and metabolic adverse effects if psychotropic medications in children and adolescents. Journal of the American Academy of Child and Adolescent Psychiatry (2006): 45(7); 771-791 8. Choice and Medication website. Accessed at:- www.choiceandmedication.org/cheshire-and-wirral/ 9. National Institute of Health and Clinical Excellence Clinical Guideline 38: Bipolar disorder 10. National Institute of Health and Clinical Excellence Technology Appraisal 213: Aripiprazole for the treatment of schizophrenia in people aged 15 to 17 years

Contents

1. Introduction

In March 2009, the National Institute of Health and Clinical Excellence (NICE) published Clinical Guideline (CG) 82 Schizophrenia. This was an update of the first Clinical Guideline, CG1, published in 2002. During the intervening years between the guidance, new evidence emerged to suggest first and second generation antipsychotics have no differences in terms of efficacy or emergence of tardive dyskinesia. The exception to this was the second generation antipsychotic clozapine, which was found to be superior in cases of treatment resistant schizophrenia. The evidence contained within NICE CG 82 caused a departure from the previous guideline, which had stated that second generation antipsychotics should be considered in the choice of first-line treatments for those newly diagnosed with schizophrenia. The updated guideline suggests any antipsychotic, first or second generation, should be considered for those newly diagnosed, for the reasons outlined above.

The aim of this policy is to advance cost-effective, evidenced-based prescribing, in line with CG 82, within Cheshire & Wirral Partnership NHS Foundation Trust and beyond. The scope of this policy is for the use of antipsychotics in psychotic illness, for example schizophrenia.

In June 2010, a multidisciplinary antipsychotic task and finish group was set up by the Medicines Management Group (MMG).

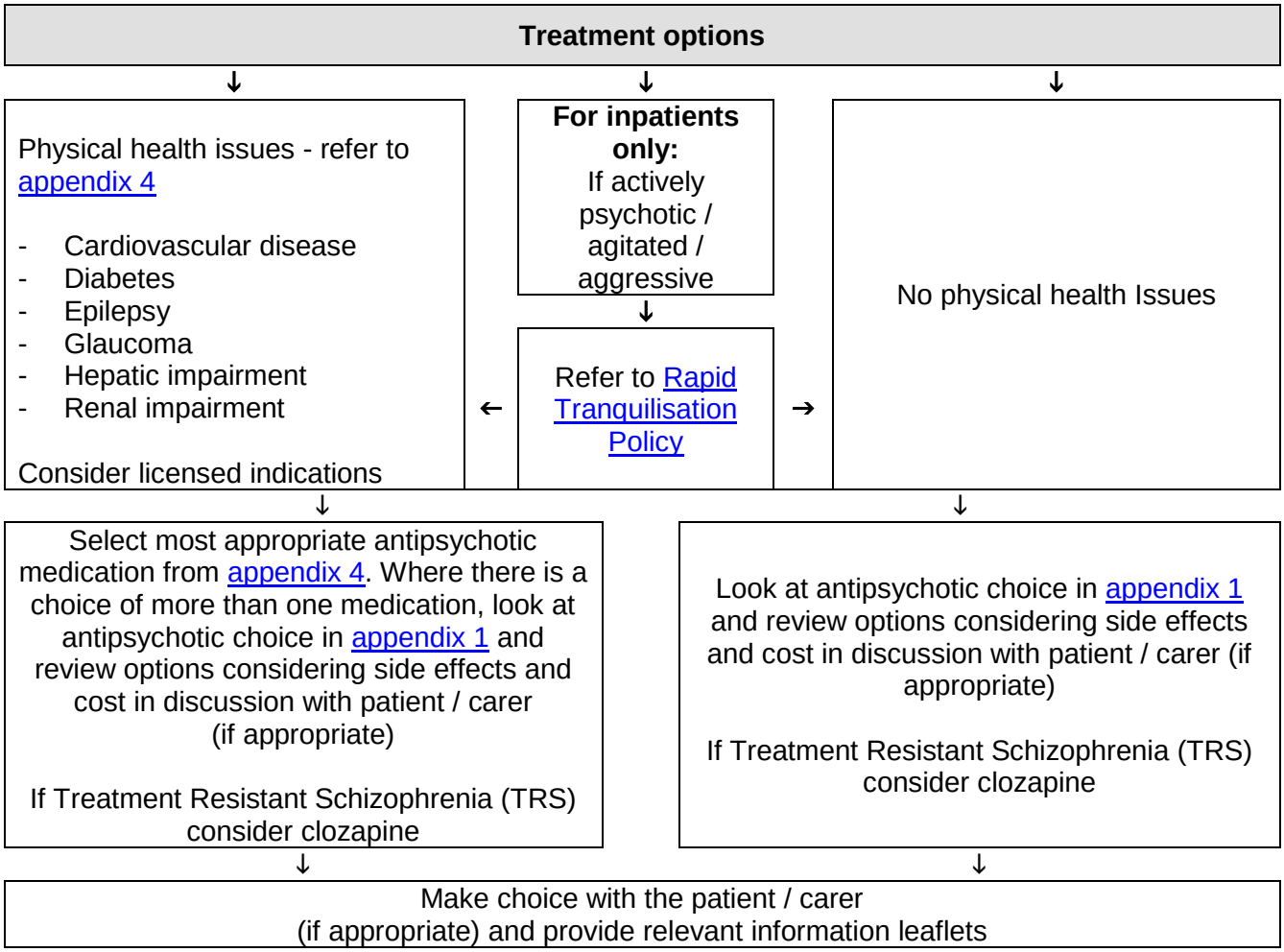
This was carried out in conjunction with the Trust's three Primary Care partner organisations. The focus of the group was to review and promote cost-effective, evidenced-based prescribing of antipsychotic medication within the CWP footprint, whilst ensuring high cost drugs are used more efficiently and appropriately.

2. Antipsychotic medication initiation pathway

The current evidence base suggests all antipsychotics have equal efficacy (with the exception of clozapine) and therefore prescribing does not need to be restricted to second generation antipsychotics. To ensure more efficient use of resources, initiation of aripiprazole, quetiapine and risperidone long acting injection will be by application, as per section 4 of this policy.

In order to aid this selection process, a table comparing antipsychotics in terms of indication, formulation, side effects and cost, is listed in appendix 1. This can be used in discussions with patients and carers, where appropriate, to promote choice and concordance with antipsychotic therapy.

2.1 Antipsychotic medication initiation pathway



3. Shared-care arrangements

Antipsychotics should be initiated and titrated as per British National Formulary recommendations.

3.1 Responsibilities of the consultant

Perform mental health assessment prior to starting antipsychotic medication, to confirm indication for treatment.

Perform baseline tests, before or as soon as possible within the first four weeks of treatment dependent upon clinical need.

These may include:

a. Weight, height (to calculate Body Mass Index), waist measurement.
b. Fasting glucose or random if not possible.
c. Fasting lipid screen or random if not possible.
d. BP, pulse.
e. ECG if indicated:
   - Patient on drugs that could prolong QT interval such as tricyclic antidepressants, quinine;
   - Patient has a history of cardiac disease;
   - Patient is an inpatient;
   - It is a recommendation in the SPC of the antipsychotic medication.

f. FBC, U&Es, LFTs, CK, Bone Profile, Prolactin (see appendix 5), TFTs. Consult local laboratory for reference ranges.

Communication between secondary and primary care should detail:

- Investigations ordered and results;
- Medication(s) stopped / prescribed and / or changes made, including dose, frequency, monitoring requirements etc;
- Indication for medication, including rationale and patient consent for off-label use;
- If the antipsychotic medication is a named-patient medication (see section 4, below), a statement should be included that approval for use has been sought and granted by the Chair of the Medicines Management Group (MMG);
- Follow up required, including care co-ordinator details and management plan.

Once the dose of the antipsychotic medication is stable, to invite the primary care prescriber to continue the prescribing by way of a letter.

3.2 Responsibilities of General Practitioner (GP)

To provide regular prescriptions for antipsychotic medications as per request after transfer of prescribing from secondary care.

To be aware of the increased risk of diabetes, cardiovascular disease and hyperlipidaemia, in patients who have schizophrenia and/or are receiving regular antipsychotics.

To monitor the physical health of the patient at least once a year, attention should be given to cardiovascular disease risk assessment as described in 'Lipid modification' (NICE clinical guideline 67) and the development of diabetes. NICE clinical guideline 82 recommends a copy of the results should be sent to the care coordinator and / or consultant, and put in the secondary care notes.

To inform secondary care of any physical health problems or deterioration of mental state, at the earliest opportunity. Prescribing responsibility may need to be transferred back to secondary care during these times.

GP to liaise with secondary care if patient suffers any adverse reaction.

4. Named-patient prescribing of oral aripiprazole, oral quetiapine and risperidone long acting injection (LAI)

4.1 Patients currently prescribed oral aripiprazole, oral quetiapine or risperidone LAI

Patients within CWP currently prescribed one of these medications will continue with their current treatment. When treatment is reviewed, and a switch is indicated (for example, due to relapse), the previous points of this policy should be considered.

4.2 Patients requiring initiation with oral aripiprazole or oral quetiapine

If a clinician believes there are extenuating circumstances as to why a patient cannot have an alternative 1st line antipsychotic which is listed in appendix 1, but requires a named-patient medication, then an application must be made to the Chair of Medicines Management Group (MMG). The letter should include a full clinical history (including diagnosis), response to previous medications and rationale for use of named-patient medication. This should be made using the appropriate appendix of introduction of new medicines.

It should be noted that the only evidence-based doses of aripiprazole are 10 and 15mg daily. Doses above 15mg must be requested in the manner stated above. They should only be considered for a time-limited period and response rated using an appropriate rating scale. If no additional benefit is obtained, the dose should be reduced back to 10 or 15mg daily.

4.3 Patients requiring initiation with risperidone LAI

In order to be considered for treatment with risperidone LAI, the patient must:

- Have been prescribed a first generation depot antipsychotic and;
- Have a history of response to, but poor compliance with, oral risperidone.

If a clinician believes the patient to meet these criteria, then an application must be made to the Chair of the MMG. The letter should include a full clinical history (including diagnosis), response to previous medications and rationale for use of named-patient medication. This should be made using the appropriate appendix of Introduction of new medicines.

Decisions regarding approval / rejection of application to use one of these medications will be communicated to the clinician within 5 working days of receipt of the application, by the Chair of the MMG.

5. Maintenance of treatment

Response and tolerability to antipsychotic medication should be reviewed to ensure optimal therapy is achieved.

The majority of patients will respond to one antipsychotic medication, polypharmacy is not recommended, which is in line with NICE guidance.

In exceptional circumstances, where a single agent has been clearly demonstrated to be inadequate, a trial of a combination of antipsychotics may be considered. The effect of the combination against targeted symptoms, and the additional side effect burden, should be carefully considered. Where no benefit is seen, therapy should revert to a single agent.

Patients receiving antipsychotic treatment should undergo close monitoring of their physical health, in line with NICE guidance.

The lowest effective dose should be used for maintenance treatment

6. Reviewing treatment

Treatment should be reviewed regularly, according to clinical need, taking into account response and tolerability to the given antipsychotic medication.

Changes to dose or switching to a different antipsychotic may be appropriate at these times.

Review of medication should be conducted in line with the Care Programme Approach (CPA).

7. Switching

Information regarding switching antipsychotics can be found in a variety of sources, such as the Maudsley Prescribing Guidelines[3] and the Psychotropic Drug Directory[4], and from the local Mental Health Pharmacist.

8. Discontinuation

If consideration is being given to the discontinuation of antipsychotic medication, advice should be sought from secondary care.

Although antipsychotics are not associated with a discontinuation syndrome as such, sudden discontinuation increases the risk of relapse. Therefore, where possible, antipsychotics should be withdrawn gradually.

9. Information for patients

There are several sources of information available for patients. The Choice and Medication website (accessed here choiceandmedication) contains patient information for the majority of psychotropic medication, including antipsychotics. CWP staff are able to print off leaflets, as requested.

As stated above, appendix 1 compares antipsychotics and may be used to aid discussion and choice. Further, a patient decision aid has been developed (see appendix 2) to promote discussions between patients and prescribers.

It should be noted that the cost of an antipsychotic is not an indicator of effectiveness, but is related to patent expiry of the antipsychotic medication.

10. Cautions

There are several cautions for the use of antipsychotic medication, such as use in those patients with pre-existing cardiovascular disease or epilepsy. For further guidance, the relevant section of the BNF and the Summary of Product Characteristics (SPC) for the specific drug should be consulted.

Particular attention should be paid to the use of antipsychotic medication in specific patient groups, such as older adults. Please see later sections of this document for further details (section 15).

11. High Dose Antipsychotic Therapy (HDAT)

HDAT is defined as:

A total daily dose of a single antipsychotic which exceeds the upper limit stated in the summary of product characteristics (SPC) or British National Formulary (BNF) and a total daily dose of two or more antipsychotics which exceeds the SPC or BNF maximum using the percentage method.

If patients are prescribed antipsychotic therapy that meets the definition of HDAT, then 'High Dose Antipsychotic Therapy (HDAT) Guideline' should be followed.

There is an expectation of clear communication between secondary and primary care, as to physical health monitoring and review of treatment, with this cohort of patients.

12. Interactions

A number of common interactions with antipsychotics can be found in appendix 3.

Caution should be exercised and extra monitoring undertaken, if any of these medications are co-prescribed with antipsychotics.

The latest edition of the BNF or the local Mental Health Pharmacist should be consulted for further details regarding interactions.

13. Prescribing antipsychotic medication in patients with pre-existing medical conditions

In appendix 4, an indication of the level of risk for a particular antipsychotic when used with a given pre-existing medical condition can be seen.

Note, this table should be used as a guide (current time valid) and more detailed up to date information can be found in the Psychotropic Drug Directory[4] or from your local Mental Health Pharmacist.

14. Pregnancy and lactation

When prescribing for patients who are pregnant or planning a pregnancy please refer to the CWP policy Guidance on the Recommended Psychotropic Agents for use in Pregnancy and Lactation and the Perinatal Pathway

15. Special patient groups

15.1 Learning disabilities

Although the use of antipsychotic medication in people with learning disabilities (LD) is a relatively common occurrence, there are specific issues relating to this patient group concerning assessment, titration and long-term treatment. Diagnosis can be difficult in people with limited language skills although this may be easier in those with a mild degree of LD if sufficient allowance is made for their reduced vocabulary. Many individuals with LD may have a concomitant behaviour disorder which may confound diagnosis, particularly where there is major impairment of social interaction.

People with LD are more likely to develop side effects with antipsychotics due to their underlying brain damage. The most common side effects are neurological , particularly extrapyramidal side effects such as Parkinsonism, dystonia, akathisia and tardive dyskinesia. People with LD are also likely to experience other side effects such as QT interval prolongation, hepatic impairment and blood dyscrasia, due to their multisystem impairment. There is good evidence in adults with normal intelligence that antipsychotics may cause sedation, psychomotor impairment and decreased ability to concentrate. These effects may be compounded in adults with LD because of the underlying organic condition.

In their study, Duggan and Brylewski (1999)[5], found no trial-based evidence for the effectiveness or ineffectiveness of any antipsychotic medication, noting that trials often exclude people with LD. The study authors concluded that until better evidence is forthcoming, clinicians will have to continue to base practice on clinical experience and evidence from the non-learning disabled population.

15.2 Child and Adolescent Mental Health (CAMHS)

15.2.1 Choice of antipsychotic medication

It should be noted that the NICE CG82 Schizophrenia covers the treatment and management of schizophrenia and related disorders in adults aged 18 years and older, and therefore excludes those below this age.

Very few antipsychotics are licensed for use in children and adolescents, and the evidence base for such use is poor.

Children and adolescents do not tolerate antipsychotics as well as adults[6,7] and so are more prone to developing / experiencing adverse events. Hence the choice of antipsychotic medication in this group of patients is particularly challenging.

The NICE technology appraisal 213 issued guidance around the prescribing of aripiprazole for young people aged 15 to 17. Aripiprazole is therefore as an option for the treatment of schizophrenia in people aged 15 to 17 years who are intolerant of risperidone, or for whom risperidone is contraindicated, or whose schizophrenia has not been adequately controlled with risperidone.

As aripiprazole is considered second-line in under 18's, it is exempt from the named-patient request status as discussed in this policy.

15.2.2 Consent in under 18 year olds

For consent purposes, over 16 year olds with capacity have the same rights as adults.

For under 16s the situation is more ambiguous, with the Mental Health Act allowing parents to consent on behalf of their children regardless of Gillick Competence. However the code of practice suggests this is not good practice.

15.2.3 Licensing of medicines

Many medications used in children and adolescents, particularly in hospital settings, are prescribed either 'off label' (outside the condition of the licence) or on an unlicensed basis (medications that have never been considered for a licence). Doctors are allowed to prescribe 'off label' and this is covered by the Medicines Act 1968 and the EC pharmaceutical directive 89/341/EEC.

15.3 Older people

The balance of risks and benefits should be carefully considered when prescribing antipsychotics in the older adult population. Further, older adult patients with dementia treated with antipsychotic drugs are at increased risk of mortality, stroke and transient ischaemic attack.
It is recommended that:

- Antipsychotic drugs should not be used to treat mild to moderate psychotic symptoms;
- Initial doses should be reduced (to approximately half the adult dose or less) and factors such as weight, co-morbidities, and concomitant medication should be considered;
- Treatment should be reviewed regularly.

Please refer to the CWP dementia pathway and the challenging behaviours document.

15.4 Bipolar disorder

The guidance within this document is specific to the prescribing of antipsychotic medications in psychotic conditions. As such, the use of antipsychotic medications in bipolar disorder will be covered elsewhere in a separate document and as per NICE CG38 Bipolar disorder[9].

16. Duties and responsibilities

16.1 Executive director for medicines management

Has the responsibility of overseeing the review and updating this policy in line with national guidance and changes in clinical practice.

16.2 Chair of medicines management group

It is the responsibility of the chair to ensure that the minutes of the meetings reflect the approval process and that all reviews of the policy are timetabled within the business cycle.

16.3 Author(s)

Responsibility to seek consultation on the policy and any updates, and then to seek approval of the policy via the appropriate trust channels. Once approved, ensuring that the policy has been disseminated appropriately and raising staff awareness of the policy.

16.4 Line managers

Have responsibility to cascade information on the revised pathway to all staff that they manage. Ensuring that any training required on the policy is included in staff's personal development plan and clinical supervision.

16.5 Trust Staff

All Trust Staff working in a clinical environment must be familiar with the policy and any subsequent updates. There is no specific training attached to this policy beyond knowledge of the national guidance and knowledge of the medicines identified within the policy.

It is the responsibility of staff to keep up to date with current practice through their individual PDPs in this area of practice.

17. Acknowledgements

Guidance on the use of antipsychotics, Sussex Partnership NHS Foundation Trust, October 2009.

Appendix 1 - Table 1: Comparison of Antipsychotic Medication

First line antipsychotic medications:

Medicine	Usual dose (per day)	Licensed indication(s)	Titration required	Formulations	Side effects					Cost (£/28 days)*
					Sedation	Muscle stiffness	Weight Gain	Dry mouth etc	Sexual problems	
Amisulpride	400 – 800mg	Schizophrenia	Yes	Tablets Liquid	•	••	••	•	•••	15.37 – 30.74
Chlorpromazine	75mg – 300mg	Schizophrenia and other psychoses Mania	No	Tablets Liquid	•••	••	••	••	•••	6.00 – 10.23
Flupentixol	6 – 18mg	Schizophrenia and other psychoses	No	Tablets	•	••	••	••	•••	3.49 – 10.47
Haloperidol	10 – 30mg	Schizophrenia and other psychoses Mania	No	Tablets Liquid Injection	•	•••	••	•	•••	4.30 – 12.90
Olanzapine	10 – 20mg	Schizophrenia Mania	No	Tablets Oro-dispersible tablets	•••	•	•••	•	•	87.40 – 158.90
Risperidone	2 – 6mg	Acute and chronic psychoses Mania	Yes	Tablets Oro-dispersible tablets Liquid	•	••	••	•	••	0.99 – 2.53
Sulpiride	400 – 1600mg	Schizophrenia	No	Tablets Liquid	•	••	••	•	•••	6.46 – 39.05
Trifluoperizine	5 – 15mg	Schizophrenia and other psychoses	No	Tablets Liquid	•	•••	••	•	•••	1.22 – 3.67
Zuclopenthixol	20 – 50mg	Schizophrenia and other psychoses	No	Tablets	••	••	•••	••	•••	3.15 – 4.04

Named-patient only:

Aripiprazole	10 – 30mg	Schizophrenia Mania	No	Tablets Oro-dispersible tablets Liquid	•	•	○	○	○	95.74 – 191.48
Quetiapine	Around 600mg	Schizophrenia Mania	Yes	Immediate Release (IR) tablets Extended Release (XL) tablets	•••	•	••	•	•	105.56 – 158.67

*Prices taken from BNF61

Depot antipsychotics:

Medicine	Usual Dose (per day)	Side effects					Cost (£/28 days)*
		Drowsiness	Muscle stiffness	Weight gain	Dry mouth etc	Sexual problems	
Flupentixol decanoate (Depixol®)	20 – 200mg every two weeks	•	••	••	••	•••	2.56 – 6.02
Fluphenazine decanoate (Modecate®)	25 – 100mg every two weeks	•	•••	••	••	•••	2.60 – 8.94
Haloperidol decanoate (Haldol®)	50 – 200mg every four weeks	•	•••	••	•	•••	3.82 – 10.12
Pipotiazine palmitate (Piportil®)	25 – 50mg every two weeks	•	••	••	••	•••	32.58
Zuclopenthixol decanoate (Clopixol®)	200 – 500mg every two weeks	••	••	•••	••	•••	3.98 – 7.30

Named-patient only:

Risperidone (Risperidal consta®)	25 – 50mg every two weeks	•	••	••	•	••	159.38 – 285.52

*Prices taken from BNF61

Third line (if the criteria for Treatment Resistant Schizophrenia is met):

Medicine	Usual dose (per day)	Licensed indication(s)	Titration required	Formulations	Side effects					Cost (£/28 days)*
					Sedation	Muscle stiffness	Weight Gain	Dry mouth etc	Sexual problems	
Clozapine	Around 200 – 600mg	Schizophrenia in patients unresponsive to, or intolerant of, conventional antipsychotic drugs	Yes	Tablets	• • •	•	• • •	• • •	•	43.12 – 129.36

*Prices taken from BNF61

Key:

• = Only a few people will get this side effect
• • = Quite a few people will get this side effect
• • • = Most people will get this side effect
° = This is very rare or not known

Table adapted from www.choiceandmedication.org

Appendix 2 - Table 2: A patient decision aid tool for antipsychotic medication*

Side effect	Incidence		
	Low	**Moderate**	**High**
Sedation	Amisulpride Flupentixol Haloperidol Risperidone Sulpiride Trifluoperazine	Zuclopenthixol	Chlorpromazine Olanzapine
Muscle stiffness	Olanzapine	Amisulpride Chlorpromazine Flupentixol Risperidone Sulpiride Zuclopenthixol	Haloperidol Trifluoperazine
Weight gain		Amisulpride Chlorpromazine Flupentixol Haloperidol Risperidone Sulpiride Zuclopenthixol	Olanzapine Trifluoperazine
Dry mouth	Amisulpride Haloperidol Olanzapine Risperidone Sulpiride Trifluoperazine	Chlorpromazine Flupentixol Zuclopenthixol	
Sexual dysfunction	Olanzapine	Risperidone	Amisulpride Chlorpromazine Flupentixol Haloperidol Sulpiride Trifluoperazine Zuclopenthixol

* Table adapted from Stephen Bazire's Psychotropic Drug Directory 2010, HealthComm UK Ltd

Incidence
Low – a few people will get this side effect
Moderate – quite a few people will get this side effect
High – Most people will get this side effect

Appendix 3 - Table 3: Common interactions with Antipsychotic Medication*

Interacting drug class	Consequences
Angiotensin-converting enzyme (ACE) inhibitors or calcium channel blockers	Risk of postural hypotension
Antiarrhythmic drugs	Increased risk of ventricular arrhythmia with antiarrhythmic drugs that prolong the QT interval such as amiodarone.
Antibacterials	Erythromycin possibly increases plasma concentration of clozapine. Ciprofloxacin increases plasma concentration of clozapine and possibly olanzapine. Plasma concentration of quetiapine possibly increased by macrolides (e.g. erythromycin).
Antidepressants	Increased risk of arrhythmias with tricyclic antidepressants. Selective serotonin re-uptake inhibitors (SSRIs) and venlafaxine increase the plasma concentration of clozapine. Fluoxetine increases the plasma concentration of haloperidol.
Antiepileptics	The threshold for convulsions is lowered. Carbamazepine reduces the plasma concentration of clozapine, haloperidol, olanzapine and risperidone. Phenytoin reduces the plasma concentration of clozapine and quetiapine. The risk of neutropenia is increased if olanzapine is given with sodium valproate.
Antivirals	Plasma concentration of clozapine possibly increased by ritonavir (avoid concomitant use) and possibly by amprenavir. Plasma concentration of olanzapine reduced by ritonavir (may need to increase dose). Plasma concentration of aripiprazole possibly reduced by efavirenz and nevirapine, metabolism of aripiprazole possibly inhibited by amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir, and saquinavir (reduce dose of aripiprazole). Plasma concentrations of antipsychotics possibly increased by ritonavir.
Lithium	Increasing lithium levels has a direct neurotoxic effect, including increased risk of neuroleptic malignant syndrome (NMS), particularly with clozapine, haloperidol and phenothiazines

* Table complied using the British National Formulary (BNF) 61, BMJ Group and Pharmaceutical Press 2011.

Appendix 4 - Table 4: Antipsychotic selection in patients with pre-existing medical conditions*

	Level of Risk of Antipsychotic Medication		
	Low	**Moderate**	**High**
Cardiovascular disease	Quetiapine Sulpiride	Amisulpride Aripiprazole Flupentixol Olanzapine Phenothiazines Risperidone Zuclopenthixol	Clozapine Haloperidol
Diabetes	Amisulpride Aripiprazole Haloperidol Risperidone Sulpiride	Flupentixol Quetiapine Phenothiazines Zuclopenthixol	Clozapine Olanzapine
Epilepsy	Amisulpride Aripiprazole Haloperidol Risperidone	Olanzapine Phenothiazines (most) Quetiapine Zuclopenthixol	Chlorpromazine Clozapine
Glaucoma (narrow-angle)	Flupentixol Haloperidol Risperidone Sulpiride Zuclopenthixol	Aripiprazole Clozapine Phenothiazines	Olanzapine
Hepatic impairment	Amisulpride Aripiprazole Flupentixol Haloperidol Sulpiride Zuclopenthixol	Clozapine Olanzapine Phenothiazines Quetiapine Risperidone	--
Renal impairment	--	Aripiprazole Clozapine Flupentixol Haloperidol Olanzapine Phenothiazines Quetiapine Zuclopenthixol	Amisulpride Risperidone Sulpiride

* Table adapted from Stephen Bazire's Psychotropic Drug Directory 2010, HealthComm UK Ltd

Appendix 5 - Hyperprolactinaemia

Dopamine receptor blockade in the tuberoinfundibular pathway can lead to increased levels of prolactin. All antipsychotics have the propensity to cause this, however some do not increase prolactin levels above the normal range at standard doses. These antipsychotic medications are: aripiprazole, clozapine, olanzapine and quetiapine. The degree of prolactin elevation is likely to be dose related. While the propensity for antipsychotic drugs to affect prolactin varies between agents, the extent to which an individual will be affected may be difficult to determine before treatment. Therefore, good practice would dictate that prolactin levels should be checked at least annually, and more frequently if indicated (e.g. if sexual dysfunction reported).

Hyperprolactinaemia often presents asymptomatically and there is evidence to suggest it does not affect quality of life. In women, hyperprolactinaemia may be associated with galactorrhoea, amenorrhoea, gynaecomastia, and decreased libido. In men, hyperprolactinaemia can cause reduced serum testosterone levels leading to decreased libido, erectile dysfunction, impotence, infertility, gynaecomastia, and rarely galactorrhoea. Sustained hyperprolactinemia may lead to decreased bone density in both female and male patients. There is also some evidence to suggest hyperprolactinaemia may be associated with an increased risk of breast cancer, although too limited as to be conclusive.

Reference ranges for prolactin levels:

	Prolactin level	
	Ng/ml	**mIU/l**
Men	0 - 20	0 – 424
Women	0 - 25	0 - 530
Re-test if prolactin concentration:	25 - 100	530 - 2120
Refer to rule out prolactinoma if prolactin concentration:	> 150	> 3180

There are various strategies that can be employed in treating hyperprolactinaemia, and it may be appropriate to refer back to Secondary Care.

Treatment options include:

- Decreasing the dose of the antipsychotic medication;
- Changing to a non-prolactin elevating antipsychotic medication;
- The addition of a dopamine agonist, such as bromocriptine or cabergoline. Caution must be excerised due to an increased risk of relapse.

Reference:

The Maudsley Prescribing Guidelines 10th Edition (2009); Taylor, Patton and Kapur; Informa Healthcare.