



Guidelines on Choice and Selection of Antipsychotics for the Management of Psychosis and Schizophrenia in Adults

Introduction

Antipsychotics are the mainstay of the pharmacological management of schizophrenia. They are used to reduce symptoms in the acute psychotic phase of the illness and also as maintenance treatment to reduce the likelihood of psychotic relapses in stable patients.

The National Institute of Health and Care Excellence (NICE) Clinical Guidelines 178 for Psychosis and Schizophrenia in Adults recommends that an oral antipsychotic be offered to individuals with newly diagnosed schizophrenia in conjunction with psychological interventions.

The aim of treatment is to improve social and cognitive functioning and patients will often require long term treatment with antipsychotic medication.

The efficacy of currently available antipsychotic agents in the treatment of schizophrenia is broadly similar^{1,2} (with the exception of clozapine's greater efficacy in treatment-resistant patients)^{1,2}. Individual patient response can however vary. Antipsychotics also have important differences in the side-effects they cause. Patients differ in the side-effects they experience and the side-effects they are willing or not willing to tolerate.

Antipsychotics are most effective in ameliorating positive symptoms of schizophrenia, but less effective in treating negative and cognitive symptoms.

Purpose and scope

To provide guidance on the choice and selection of antipsychotic medication for the management of psychosis and schizophrenia within Hertfordshire Partnership University NHS Foundation Trust (HPFT).

These guidelines cover both first episode psychosis and subsequent episodes and are based primarily on [NICE CG 178 Psychosis and schizophrenia in adults](#).

These guidelines do not cover the management of psychoses and schizophrenia in:

- Children and adolescents [NICE CG 155 Psychosis and schizophrenia in children and young people](#)
- Pregnancy and lactation [NICE CG 192 Antenatal & postnatal mental health: clinical management and service](#).

They also do not cover the use of antipsychotics in management of other disorders; please consult relevant national and/or local guidelines or contact Pharmacy for specific advice.

This document does not aim to provide full prescribing guidelines and other relevant sources of information (see below) and HPFT policies should be consulted for guidance on the safe and effective prescribing of antipsychotics. This is in addition to the above NICE Clinical Guidelines:

- British National Formulary (BNF)
- Summary of product characteristics (SPC)
- Maudsley Prescribing Guidelines in Psychiatry
- Psychotropic Drug Directory
- Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology
- HPFT Clozapine Policy
- HPFT High Dose Antipsychotic Therapy (HDAT) Guidelines
- HPFT Physical Health Policy
- HPFT Rapid Tranquillisation Policy
- HPFT Management of Behavioural and Psychological Symptoms of Dementia
- HPFT Medicines Adherence Policy

General principles^{3,4}

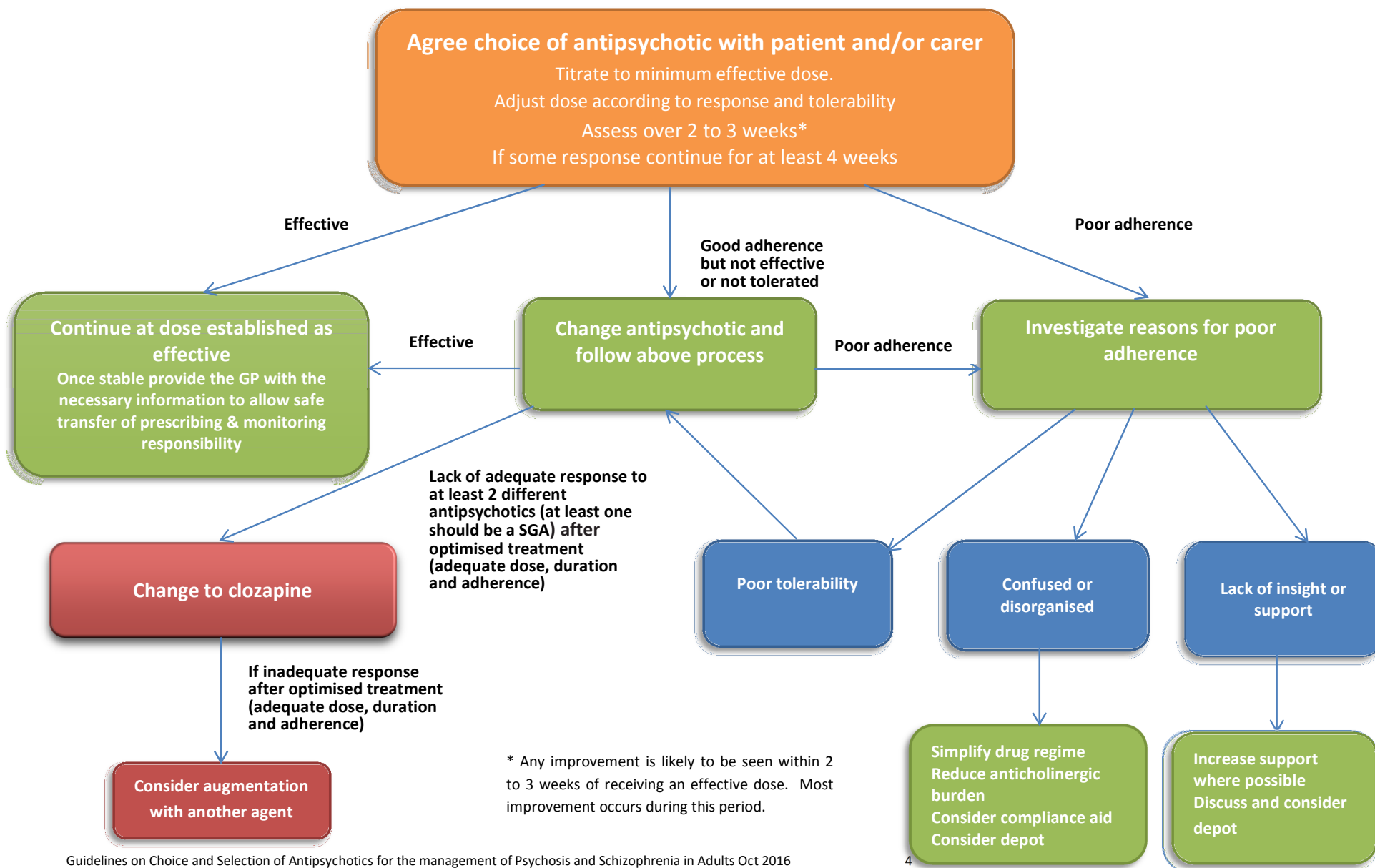
- With the exception of clozapine, the efficacy of all antipsychotics is very similar and the initial choice should be based on several factors. These are listed under “Choice of Antipsychotic” below.

[Note: Clozapine is indicated in treatment-resistant schizophrenia and should only be used when there has been a lack of satisfactory clinical improvement despite the use of adequate doses of at least two different antipsychotic agents, including an atypical antipsychotic agent, prescribed for adequate duration. Clozapine is also licensed for use in psychotic disorders occurring during the course of Parkinson's disease, in cases where standard treatment has failed].

- An individual trial of the antipsychotic of choice should be conducted in terms of dosage, duration (up to 4 weeks at optimum dosage) and medication adherence.
- Record the indications and expected benefits and risks of oral antipsychotic medication. Also document the expected time for a change in symptoms and emergence of side-effects.
- Discuss and record the side-effects that the person is most willing to tolerate.
- At the start of treatment, use doses at the lower end of the licensed range and slowly titrate upwards according to response and tolerability. Assess response (at optimum dosage) over 2 to 3 weeks, and if some response continue for at least 4 weeks before considering a change of drug. See treatment algorithm on page 4. The lowest effective dose should be used. Doses should be within the maximum BNF or SPC dose limits.
- Lower doses are particularly appropriate for negative symptoms and first episode psychosis.
- Record the rationale for continuing, changing or stopping medication, and the effects of such changes. Communicate this to the GP especially when prescribing responsibility is to be transferred to primary care.
- Current evidence does not justify the routine use of High Dose Antipsychotic Therapy (HDAT). Justify and record the reasons for prescribing dosages outside the range given in the BNF or SPC. Refer to HPFT HDAT Guidelines.

- Patients should only be treated with ONE regular antipsychotic at a time except in exceptional circumstances (e.g. clozapine augmentation or when cross-tapering medication). Antipsychotic polypharmacy should be avoided due to increased risk of adverse effects such as extrapyramidal side effects (EPSEs), QT interval prolongation and sudden cardiac death⁵.
- Oral and parenteral doses of the same antipsychotic should be prescribed separately as they can vary in bioavailability.
- As required prescriptions should be reviewed regularly, ideally weekly, or as appropriate for clinical indication, frequency of administration, therapeutic benefits and side-effects. Prescriptions that are no longer required should be cancelled and doses of regular antipsychotics adjusted accordingly where appropriate. Check whether when required prescriptions have led to a dosage above the maximum daily dose specified in the BNF or SPC.
- Response to treatment and side-effects experienced should be assessed using validated rating scales and recorded in the electronic patient record (EPR).
- There should be a clear plan in the patient's clinical records regarding on-going prescribing and monitoring requirements (including physical health checks). This should be clearly communicated to the GP when prescribing and monitoring responsibilities are transferred to primary care.
- The use of orodispersible tablets and liquid formulations should be regularly reviewed and changed to oral solid dosage formulations whenever possible.

Algorithm for the pharmacological management of schizophrenia



Choice of antipsychotic^{3,4}

- No single antipsychotic is routinely recommended as first choice in the treatment of schizophrenia or psychosis, as no single antipsychotic has superior efficacy (excluding clozapine) and response and tolerability to each antipsychotic varies.
- The decision on which antipsychotic to prescribe should be made jointly by the prescriber and service user/carer(s) and should be guided by:
 - patient's clinical presentation
 - any general medical/physical health conditions
 - any concurrent medication
 - the antipsychotics' side-effect profile including metabolic, extrapyramidal, cardiovascular, hormonal side-effects and other side-effects including unpleasant subjective experiences (see Appendix 1)
 - patient's previous response to any antipsychotics
 - patient's previous tolerance of any antipsychotics (including unpleasant subjective experiences)
 - side-effects the patient is most willing to tolerate
 - any contra-indications and cautions
 - patient's preference
 - cost-effectiveness
- The '[Choice and Medication](#)' website has a number of [Handy Charts](#) which may help the prescriber and patient/carer(s) decide which antipsychotic is the most suitable.
- When discussing treatment options with patients /carer(s), written information should be provided along with information about how to access further information if needed. Patient information leaflets are available from [Choice and Medication](#) website.

Side-effects

- Antipsychotics have different side-effect profiles (see Appendix 1)⁷. The adverse effects of particular note are the propensity for first generation antipsychotics (FGA) to cause extra pyramidal side-effects (EPSEs) including akathisia and the varying propensity for many of the FGAs and some second generation antipsychotics (SGAs) to cause weight gain, hyperprolactinaemia and metabolic sequelae such as diabetes and lipid disturbances.
- Not all patients experience EPSEs. Anticholinergic drugs should ideally be prescribed on a when required basis if and when EPSEs such as Parkinsonism and dystonias occur and should not be used to manage tardive dyskinesia as they can exacerbate this symptom. Most patients do not require anticholinergics long-term and withdrawal should be attempted if the patient is no longer experiencing troublesome side-effects. It is important to avoid increasing the anticholinergic burden where possible, especially in older adults, as medicines with an anticholinergic effect can impair cognition, increase the risk of falls, as well as causing other side-effects⁶.
- SGAs may be preferable in the treatment of first episode psychosis due to lower propensity for EPSEs within BNF dose range.
- Venous thromboembolism and neuroleptic malignant syndrome are rare but potentially fatal side-effects of all antipsychotic drugs.

- Persistent elevation of plasma prolactin is associated with sexual dysfunction, reductions in bone mass density, menstrual disturbances, breast growth and galactorrhoea and possible increase in risk of breast cancer. Prolactin elevating drugs should be avoided if possible in patients under 25 years of age i.e. before peak bone mass, with osteoporosis or with a history of hormone dependent breast cancer. In symptomatic patients consider switching to an alternative antipsychotic (see table 3). If asymptomatic discuss implications with patient and make a joint decision to stay on current treatment or switch to another antipsychotic.

- Antipsychotics also vary in the degree of cardiac risk including, arrhythmias, syncope, QT prolongation, Torsade de pointes (potentially life threatening heart arrhythmia) and sudden cardiac death. In order to reduce the risk of QT prolongation the following is recommended:
 - Use minimum effective dose
 - Avoid polypharmacy
 - Avoid concomitant prescribing of more than one drug that prolongs QT interval
 - Avoid hepatic enzyme inhibitors
 - Correct any modifiable risk factors e.g. electrolyte imbalances
 - Perform baseline ECG before starting antipsychotic medication if:
 - specified in the summary of product characteristics (SPC). See table 1 below
 - a physical examination has identified specific cardiovascular risk (such as diagnosis of high blood pressure)
 - there is a personal history of cardiovascular disease /disorder or
 - the service user is being admitted as an inpatient

Repeat ECG if clinically indicated eg after dose increase/titration, at annual check-up (if previous abnormality, presence of cardiovascular risk or additional risk factors) or high dose antipsychotic is prescribed. Perform annual ECG if clozapine dose >600mg/day or otherwise indicated.

Antipsychotics which have baseline ECG specifically recommended in SPC

Antipsychotic	Wording in SPC under Special precautions and warnings
Haloperidol (moderate effect on QTc)	A baseline ECG is recommended before treatment. During therapy, the need for ECG monitoring for QTc interval prolongation and for ventricular arrhythmias must be assessed in all patients. Whilst on therapy, it is recommended to reduce the dose if QTc is prolonged, but haloperidol must be discontinued if the QTc exceeds 500 ms. Electrolyte disturbances such as hypokalaemia and hypomagnesaemia increase the risk for ventricular arrhythmias and must be corrected before treatment with haloperidol is started. Therefore, baseline and periodic electrolyte monitoring is recommended.
Chlorpromazine (moderate effect on QTc)	Where clinically possible, the absence of any factors favouring the onset of ventricular arrhythmias should be ensured before administration: bradycardia less than 55 beats per minute; hypokalaemia; congenital long QT interval; ongoing treatment with any drug which could induce marked bradycardia (<55 beats per minute), hypokalaemia, intracardiac conduction depression or QT prolongation. With the exception of emergencies, it is recommended that the initial work up of patients receiving a neuroleptic should include an ECG.
Clozapine (low effect on QTc)	Patients with history of cardiac illness or abnormal cardiac findings on physical examination should be referred to a specialist for other examinations that might include an ECG, and the patient treated only if the expected benefits clearly outweigh the risks (see section 4.3). The treating physician should consider performing a pre-treatment ECG.

Interactions

- Consider the impact of antipsychotic interactions with other medicines. Important drug interactions⁸ are listed in Appendix 3. The hydrocarbons from cigarette smoking can also induce liver enzymes and affect plasma levels of certain antipsychotics, particularly clozapine and olanzapine. Please refer to HPFT Nicotine Replacement Policy for further information and guidance on managing the impact cigarette smoking and changes in smoking habit can have on antipsychotic plasma levels.

Clozapine

- Clozapine should be introduced at the earliest opportunity in patients with evidence of treatment resistant schizophrenia ie those whose illness has not responded adequately to treatment despite the sequential use of adequate doses of at least two different antipsychotic drugs. At least one of these drugs should be a second-generation antipsychotic³. Measuring plasma clozapine levels can be a useful tool to monitor adherence and maximise efficacy and minimise side-effects
- Augmenting clozapine with another agent occasionally needs to be considered when there has been a poor or inadequate response to clozapine alone. The evidence base supporting augmentation is limited and at best shows a marginally improved response. Augmentation should only be considered once clozapine treatment has been optimised, ensuring adequate dose, duration of treatment and adherence. Efficacy of clozapine augmentation should be assessed using recognised scales and clozapine should be discontinued if there is an unsatisfactory response after a suitable trial period e.g. 3 to 6 months⁹. Contact Pharmacy department for advice on options to augment clozapine treatment.

Monitoring

- Baseline physical health monitoring should be performed at the start of antipsychotic treatment as outlined in the HPFT Physical Health Policy (see appendix 2) and as recommended in the SPC.
- When prescribing maintenance therapy, prescribers should ensure that on-going physical health is monitored in accordance with HPFT Physical Health Policy and SPC. Prescribers must respond to any abnormal results appropriately (see appendix 2). [The Lester Positive Cardiometabolic Health Resource](#) provides clinicians with a simple assessment and intervention framework to protect the cardiovascular and metabolic health of patients with severe mental illness receiving antipsychotic medication.

Switching

- Antipsychotics may need to be switched for a variety of reasons or they may even need to be stopped altogether. There are risks associated with switching or stopping antipsychotics, such as cholinergic rebound, withdrawal dyskinesias, relapse or destabilisation⁷ and how this is managed will very much depend on the reason for the change as well as the antipsychotics involved and individual patient factors. Please refer to the latest editions of the Psychotropic Drug Directory and or The Maudsley Prescribing Guidelines in Psychiatry for further information or contact The Pharmacy Team for specific advice on this.

HPFT formulary antipsychotics

Table 1 lists the antipsychotics and the formulations available on the Trust formulary. If a clinician wishes to use an antipsychotic or a formulation of an antipsychotic which is not listed, then a [new drug application](#) will need to be made to either include this on the formulary if it is to be used more widely, or for named patient use only.

Table 1 Antipsychotic formulations on HFPT Medicines Formulary

First Generation	Available Formulations	Comments
Chlorpromazine	25mg, 50mg and 100mg tablets 25mg/5ml and 100mg/5ml oral solution	Can cause skin photosensitivity
Flupentixol (dihydrochloride)	500microgram, 1mg and 3mg tablets	Last dose to be taken before 4pm (500 microgram and 1mg tablets only licensed for depressive illness)
Haloperidol	500microgram capsules/tablets 1.5mg, 5mg, 10mg, tablets 1mg/ml and 2mg/ml oral solution (sugar free) 5mg/ml injection	See DTC recommendation on haloperidol and ECG monitoring
Sulpiride	200mg and 400mg tablets 200mg/5ml oral solution	Caution in aggressive, agitated or excited patients (even low doses aggravate symptoms)
Trifluoperazine	1mg and 5mg tablets 1mg/5ml and 5mg/5ml oral solution	EPSEs more frequent especially at doses above 6mg daily. All formulations very costly (£63 for 56 x 5mg) compared to SGA formulations.
Zuclopenthixol (dihydrochloride)	2mg and 10mg and 25mg tablets	
Second Generation	Formulation	Comments
Amisulpride	50mg, 100mg, 200mg, 400mg tablets 100mg/ml oral solution	Significantly higher cost than other SGA generic solid dose forms.
Aripiprazole	5mg, 10mg, 15mg, 30mg tablets 10mg and 15mg orodispersible tablets 1mg/1ml oral solution 7.5mg/ml injection	Orodispersible tablets are restricted for use in those with swallowing difficulties or problems with concordance. Oral solution is very expensive - only to be used when titrating doses or for doses less than 5mg. Transfer to plain or orodispersible tablets where possible.
Clozapine	25mg and 100mg tablets only 50mg/ml oral suspension	Prescribing to remain within HPFT. See Clozapine Policy. Suspension can settle on standing - risk of uneven distribution of clozapine and inaccurate dosing if bottle is not shaken thoroughly

		before measuring dose. Only to be used in those with swallowing difficulties or poor compliance.
Olanzapine	2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg tablets 5mg, 10mg, 15mg, 20mg orodispersible tablets RESTRICTED USE Velotabs® 5mg, 10mg, 15mg, 20mg Olanzapine 10mg injection (unlicensed)	Orodispersible tablets should be reserved for use in those unable to swallow solid dose forms or problems with concordance. There are slight variations in the speed at which generic orodispersible tablets dissolve in the mouth. It may be necessary to prescribe Velotab® brand if there is a problem with a service user removing generic orodispersible tablets from their mouth. Velotabs® are significantly more costly than generic tablets or orodispersible tablets.
Quetiapine	25mg, 100mg, 150mg, 200mg, 300mg tablets RESTRICTED USE 50mg, 150mg, 200mg, 300mg, 400mg XL (modified release tablets)	XL tablets should only be prescribed for: - acutely unwell patients for first 3 days after which immediate release (IR) tablets should be prescribed - those who cannot tolerate the switch to IR tablets once or twice a day - those in whom it would be clinically inappropriate to use or switch to IR tablets – a valid reason must be provided. See quetiapine briefing
Risperidone	500micrograms, 1mg, 2mg, 3mg, 4mg tablets 500micrograms, 1mg, 2mg, 3mg, 4mg orodispersible tablets 1mg/ml oral liquid	Dose response studies suggest doses above 6mg daily generally provide no additional benefit but increased risk of side effects such as EPSEs and raised prolactin ⁵ . Orodispersible should be reserved for use in those unable to swallow solid dose forms or problems with concordance.

Antipsychotics that have NOT been approved

Asenapine tablets

Paliperidone tablets

Lurasidone tablets

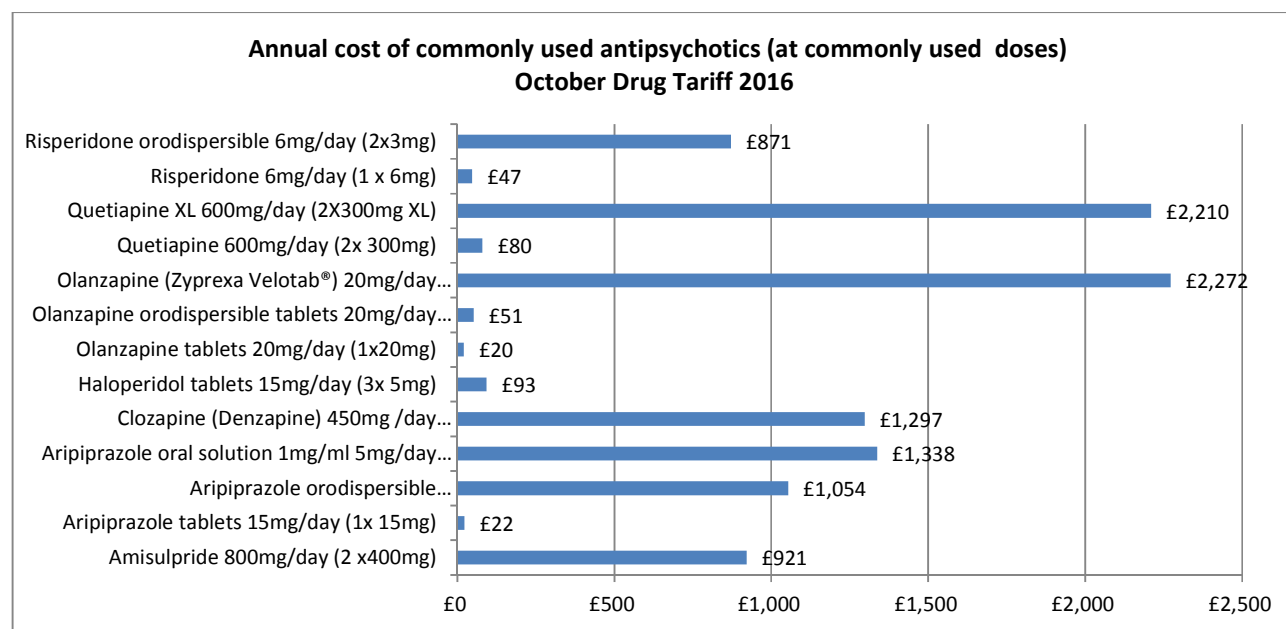
Oral Antipsychotic Costs

- All antipsychotics should be prescribed by generic name, unless there is a clinical reason to prescribe olanzapine orodispersible as Velotabs® which should be documented as described in table 1
- Orodispersible and liquid formulations are significantly more expensive than standard tablet or capsule formulations and therefore should be reserved for use in those unable to swallow solid dose forms or problems with concordance. Their use should be reviewed regularly.

- Drug costs must not be viewed in isolation as their benefit in preventing relapse can significantly outweigh the cost associated with management and treatment of a relapse.

Graph 1

Comparative annual costs of oral antipsychotics at commonly used doses (Drug Tariff Oct 2016)



Antipsychotic Long Acting Injections (LAIs)

- The term Long Acting Injection (LAI) in these guidelines refers to both conventional oil based depots which are predominantly FGAs and the newer SGA long acting injections.
- LAIs are a useful option when concordance with oral antipsychotic treatment is unreliable.
- The FGA LAIs are licensed for the maintenance treatment of schizophrenia and other psychoses whereas the SGA LAIs are licensed for maintenance treatment of schizophrenia in those who have been stabilised with the oral formulation. (Paliperidone LAI can also be used in patients previously responsive to oral paliperidone or risperidone).
- Consider offering an antipsychotic LAI to people with psychosis or schizophrenia
 - who would prefer such treatment after an acute episode
 - where avoiding covert non-adherence (either intentional or unintentional) to antipsychotic medication is a clinical priority within the treatment plan⁵
- It is preferable to maintain the same antipsychotic when switching from oral to LAI in those who have shown some response to the oral form, however not all antipsychotics are available as LAI and the clinical pharmacy team can be contacted for advice on alternative choices of LAI when required
- As with oral antipsychotics, FGA LAIs have a higher propensity for EPSEs whilst SGA LAIs have a relatively lower propensity for this side-effect at therapeutic doses.
- There is no evidence of any greater benefit with SGA LAIs over FGA LAIs in preventing relapses or admission to hospital. There are however significant price differences between the two groups of LAIs. FGA LAIs should be considered first as they are significantly cheaper

and only if not clinically appropriate or not tolerated should a SGA LAI be selected. A clear rationale for selecting a SGA over FGA must be documented.

- See [Guidance on the Administration to Adults of Oil-based Depot and other Long-Acting Intramuscular Antipsychotic Injections](#) and HPFT injections procedure.

Table 2 Formulary Long acting injections

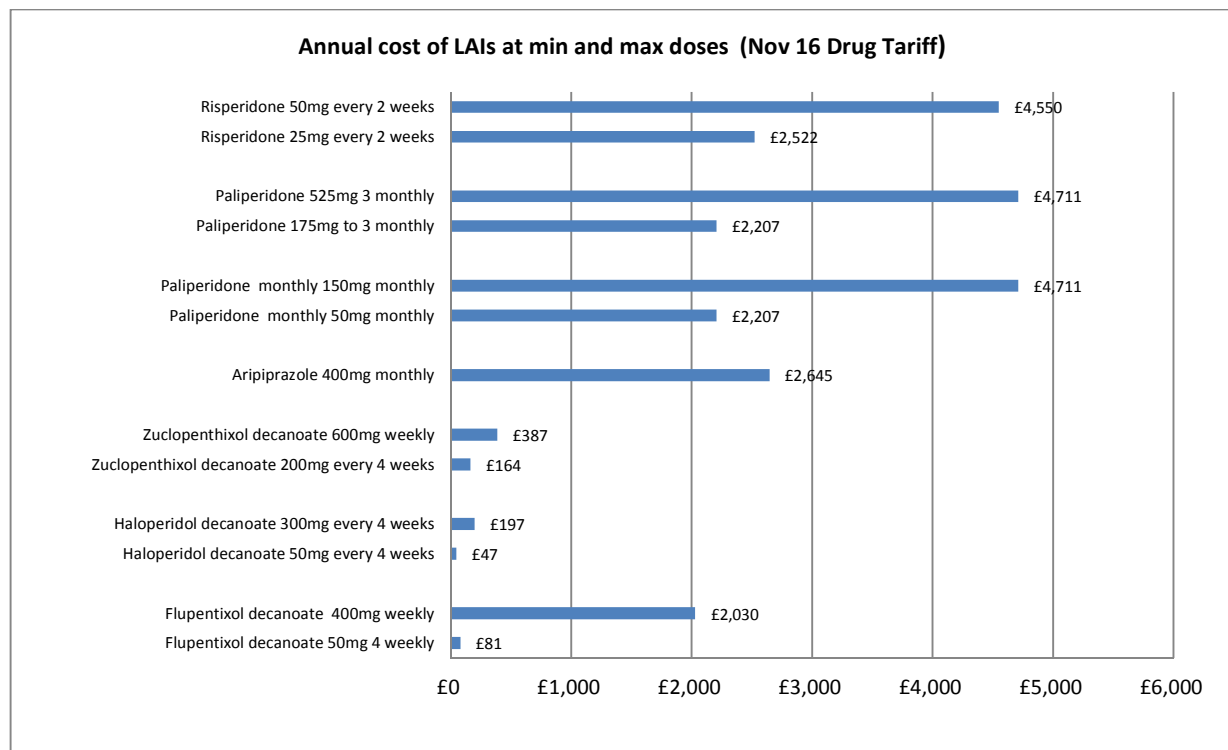
First Generation	Formulation	Comments
Flupentixol decanoate	40mg/2ml, 100mg/ml, and 200mg/ml injection ampoule	Every 2 to 4 weeks Avoid in excitable and overactive patients
Haloperidol decanoate	50mg/ml and 100mg/ml	Every 4 weeks
Zuclopenthixol decanoate	200mg/ml and 500mg/ml	Every 1 to 4 weeks May be more suitable in agitated /aggressive patients
Second Generation	Formulation	Comments
Aripiprazole (Abilify Maintena®)	300mg and 400mg powder and solvent for suspension for injection vials	Monthly <ul style="list-style-type: none"> ▪ For patients stabilised on oral aripiprazole ▪ Continue oral for 14 consecutive days after first injection ▪ Good choice of treatment for <ul style="list-style-type: none"> - when FGA LAI or paliperidone LAI cannot be used (e.g. not tolerated or contra-indicated) - first episode psychosis - metabolic disturbance with previous antipsychotics ▪ Check for drug interactions which may require dose adjustment
Paliperidone palmitate (Xeplion®)	50mg/0.5ml 75mg/0.75ml 100mg/ml 150mg/1.5ml pre-filled syringes	Monthly <ul style="list-style-type: none"> ▪ Consider when FGA LAI is not tolerated or is not clinically appropriate ▪ Paliperidone is the active metabolite of risperidone. ▪ Patients must be stabilised on oral risperidone (or paliperidone). ▪ In selected patients with previous responsiveness to oral risperidone (or paliperidone), paliperidone LAI may be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed. See Guidance on Prescribing and Administration ▪ May increase prolactin levels and has a similar side-effect profile to risperidone.

Paliperidone palmitate (Trevicta®)	175 mg, 263 mg, 350 mg, 525 mg prolonged release suspension for injection	3 monthly. (NAMED PATIENT REQUEST – for evaluation of patient experience) <ul style="list-style-type: none"> ▪ Consider in those who are adequately treated with 1-monthly paliperidone palmitate injectable and on a stable dose for a minimum of 6 months or more at the same dose.
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Note:

- Risperidone LAI is no longer included in the trust medicines formulary as there are no clinical or practical advantages of using this over paliperidone LAI. Existing patients can remain on this preparation, however any new patients for whom formulary LAI choices are not suitable and risperidone LAI is deemed to be the most appropriate choice then an application to use this on a [named patient basis](#) must be made by the consultant.
- Olanzapine embonate LAI is NOT approved. It's use must be requested on a named patient basis.

Graph 2 Comparative annual costs of LAIs at min and max doses (Drug tariff Nov 2016)



Antipsychotic choice in certain situations

Patients will often experience intolerable side-effects from antipsychotics and the table below gives some suggestions on possible alternative choices of antipsychotics in these situations.

Table 3 Suggested choices of antipsychotics when poor tolerability due to side-effects⁴

Adverse effect	Suggested drugs	Alternatives
Acute extrapyramidal symptoms	Aripiprazole Olanzapine Quetiapine	Clozapine*
Dyslipidaemia	Amisulpride Aripiprazole	
Impaired glucose tolerance	Amisulpride Aripiprazole	Haloperidol Risperidone
Hyperprolactinaemia	Aripiprazole Quetiapine	Clozapine* Olanzapine
Postural hypotension	Amisulpride Aripiprazole	Haloperidol Sulpiride Trifluoperazine
QT prolongation	Aripiprazole	Low dose monotherapy of any drug not formally contra-indicated in QT prolongation
Sedation	Amisulpride Aripiprazole Risperidone Sulpiride	Haloperidol Trifluoperazine
Sexual Dysfunction	Aripiprazole Quetiapine	Clozapine*
Tardive Dyskinesia	Clozapine*	Aripiprazole Olanzapine Quetiapine
Weight gain Lifestyle advice and support	Amisulpride Aripiprazole Haloperidol	Risperidone Quetiapine Trifluoperazine

*Clozapine is only an option if lack of satisfactory clinical response to at least two different antipsychotics (at least one should be a SGA) after optimised treatment (adequate dose, duration and adherence).

Older Adults (>60 years)

NICE CG guideline 178 covers the treatment and management of psychosis and schizophrenia and related disorders in adults (18 years and older) with onset before 60 years. Antipsychotics, however, are often required for the management of such disorders in people aged over 60. Due to changes in pharmacodynamic sensitivity and pharmacokinetics, older adults are more sensitive to side-effects of medicines and this can result in an increase in the incidence and severity of adverse effects. The balance of risks and benefit should be considered before prescribing antipsychotic drugs for older adults.

In people with dementia, antipsychotic drugs are associated with a small increased risk of mortality and an increased risk of stroke or transient ischaemic attack¹⁰. See [HPFT Management of behavioural and psychological symptoms of dementia](#).

Furthermore, older adults are particularly susceptible to postural hypotension which can lead to falls.

To reduce drug related risk it is recommended that⁴

- Antipsychotic drugs should only be used in older adults when absolutely necessary.
- Initial doses of antipsychotic drugs in older adults should be reduced (to half the adult dose or less), taking in to account factors such as the patient's weight, co-morbidity, and concomitant medication.
- Avoid if possible drugs that block alpha1 adrenoceptors, have anticholinergic side-effects, are very sedative, have a long half-life or are potent inhibitors of hepatic metabolising enzymes.
- Treatment should be reviewed regularly.

Older adults often receive multiple medicines for their multiple diseases and this can greatly increase the risk for drug-drug and drug-disease interactions.

NOTE: Some of the links in this document may not be accessible to non-HPFT staff. Please contact the Pharmacy department for access to these.

Transfer of APD prescribing to GPs

Patients must be stabilised on an APD before requesting the GP to take over prescribing responsibility. The following **minimum** information must be provided to enable the GP to safely take on the continued prescribing for the patient:

- **Choice of APD:** including formulation and dose.
- **Rationale for choice of APD:** The rationale for continuing, changing or stopping medication. Where relevant include details of APDs that have already been tried and why they were discontinued or not appropriate.
- **Monitoring requirements:** as per physical health policy.
- **Date of next review**
- **Prescriber contact details:** in case GP has any queries or concerns.

Clinicians must ensure all the above information is included in correspondence to GPs to ensure the smooth and safe transfer of prescribing responsibility.

References

1. Jones P.B, *et al.* Randomised controlled trial of the effect on quality of life of second-vs. first-generation antipsychotic drugs in schizophrenia. Cost utility of the latest antipsychotic drugs in schizophrenia study (CUtLASS-1). *Arch Gen Psychiatry* 2006; 63: 1079-87.
2. Lieberman J., Stroup T.S, McEvoy J., *et al.* (Clinical Antipsychotics Trials of Intervention Effectiveness [CATIE] Investigators). Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005; 353(12): 1209-23.
3. NICE Clinical Guideline 178. Psychosis and schizophrenia in adults: treatment and management. (2014) National Institute for Health and Care Excellence (NICE).
4. The South London and Maudsley NHS Trust Prescribing Guidelines, 12th edition
5. Consensus Statement on High Dose Antipsychotic Medication. Council Report CR138.2006. Royal College of Psychiatrists, London.
6. Fox C, Richardson K, Maidment ID, *et al.* Anticholinergic medication use and cognitive impairment in the older population; the Medical Research Council Cognitive Function and Ageing Study. *Journal of the American Geriatrics Society* 2011;59:1477–83.
7. Psychotropic Drug Directory, 2012, S Bazire, HealthcommUK Ltd.
8. [Important drug interactions, MRHA Antipsychotics Learning Module Feb 2015](#)
9. Clozapine Handbook. S Bleakley, D Taylor 1st Edition Lloyd-Reinhold Communications
10. Banerjee S. The use of antipsychotic medication for people with dementia: time for action. A report for the Minister of State for Care Services London: Department of Health, 2009.

Appendices

Appendix 1 - Antipsychotic relative side-effects table.

Appendix 2 - Recommended Routine Physical Health Monitoring for Service Users.

Appendix 3- Important drug interactions with antipsychotics.

Appendix 1

Antipsychotics relative side-effects⁹

The following table can be used by prescribers in conjunction with patients to help guide choice of APD. Alternatively the [Choice and Medication](#) website provides information for patients on medicines used in mental health. The [handy chart](#) comparing medicines used for psychosis is a more patient friendly resource which may be helpful when discussing potential benefits and harms of individual antipsychotics with patients. Please note the Choice and Medication website may include information on medicines that have not been approved in Hertfordshire.

FGA	Anticholinergic effects	Cardiac	EPSE	Hypotension	Sedation	Weight gain	Prolactin elevation	Proconvulsant
Chlorpromazine	●●	●●	●●	●●●	●●●	●●●	●●●?	●●●
Haloperidol	●●	●●	●●●	●	●	●	●●●	●?
Flupentixol	●●	○	●●	○	●	●	●●?	●?
Sulpiride	●	○	●	○	●	●	●●	○?
Trifluoperazine	●●●	●●	●●	●	●	?	●●●?	●
Zuclophenthixol	●●	●	●●●	●	●●	?	●●?	○?
SGA	Anticholinergic effects	Cardiac	EPSE	Hypotension	Sedation	Weight gain	Prolactin elevation	Proconvulsant
Amisulpride	●●	○	●	○	○	●	●●	●?
Aripiprazole	○	●	●	○	○	●	○	○
Clozapine	●●	●●●	○	●	●●●	●●●	○	●●●
Olanzapine	●	○	○	○	●●	●●●	●	●●
Quetiapine	●	●	○	●	●●	●	●	●
Risperidone	●	○	●	●	●?	●	●●	○
FGA Depot injections	Anticholinergic effects	Cardiac	EPSE	Hypotension	Sedation	Weight gain	Prolactin elevation	Proconvulsant
Flupentixol	●●	○	●●	○	●	?	●●?	●?
Fluphenazine	●●	●●	●●●	●	●●	●	●●●?	●
Haloperidol	●	●●	●●●	●	●	●	●●●	●
Zuclophenthixol	●●●	●	●●●	●	●●	?	●●?	○?
SGA Long acting injections	Anticholinergic effects	Cardiac	EPSE	Hypotension	Sedation	Weight gain	Prolactin elevation	Proconvulsant
Aripiprazole	○	●	●	○	○	●	○	○
Paliperidone	○	○	●	●	●	●	●●	○

●●● marked effect ●● moderate effect ● mild/ transient effect ○ little or minimal effect ? no information available or little reported

Reference: Stephen Bazire – Psychotropic Drug Directory 2016

Appendix 2

Recommended Routine Physical Health Monitoring for Service Users¹¹

See [HPFT Physical Health Policy Version 5](#)

Table 1

		Baseline	3 months if antipsychotic initiated	6 months if antipsychotic initiated	Annual Review/ Health check
a	Personal and Family History	✓			
b	Smoking	✓	✓	✓	✓
c	Alcohol and Drug Use	✓			✓
d	Allergies/Drug sensitivities	✓			
e	Exercise and dietary habits	✓	✓	✓	✓
f	Dental Health	✓			✓
g	Weight (BMI/Waist circumference) Ideally plotted on a chart	✓	✓ *	✓	✓
h	Blood pressure	✓	✓	✓	✓
i	Blood lipid profile and fasting (if possible) plasma glucose /HbA1c Consider other relevant blood tests or investigations required	✓	✓	✓	✓
j	Sexual health and contraception. Consider the need for a pregnancy test	✓			
k	Check engagement with Primary Care	✓			✓
l	Screen for side-effects (including sexual)		✓	✓	✓
m	Offer information about medication	✓	✓	✓	✓
n	Health Promotion and Signposting where appropriate	✓			✓

*NICE CG 178 for Schizophrenia recommends measuring weight weekly for first 6 weeks (plotted on a chart)

Frequency of review: As a minimum review those prescribed a new antipsychotic at baseline, at least once after 3 months, at 6 months and annually thereafter. For some medicines more frequent monitoring may be required. See table 2 for details on monitoring for specific drugs. Health checks should take place at least annually unless an abnormality of physical health emerges. In these cases, appropriate action should be taken and/or the situation should be reviewed at least every 3 months.

See [Positive Cardiometabolic Health Resource](#) for monitoring individuals commenced on antipsychotics.

Diagnosis/Psychotropic Drugs Requiring Specific Tests¹¹

In addition to the monitoring outlined in table 1 some drugs require more specific tests/monitoring. The recommendations below are best practice guidelines.

Table 2

DIAGNOSIS	BASELINE	MAINTENANCE
Serious Mental Illness (psychosis/bipolar disorder)	Full Blood Count (FBC) Urea and Electrolytes (U&Es) Renal function (serum creatinine or e-GFR) Liver Function Tests (LFTs) Fasting blood glucose (if possible), HbA _{1c} Blood lipid profile (fasting if possible) Prolactin level ECG if clinically indicated BP, weight, waist circumference	Annual health check* FBC annually U&Es annually Renal Function (serum creatinine or e -GFR) annually LFTs annually Fasting (if possible) blood glucose, HbA _{1c} annually Blood lipid profile (fasting if possible) annually
DRUG		
Antipsychotics		
Amisulpride Aripiprazole Olanzapine Quetiapine Risperidone First generation antipsychotics	FBC Fasting (if possible) blood glucose, HbA _{1c} baseline then at 3 months and 1 year (olanzapine also at 1 month and 6 month) Blood lipid profile baseline then at 3 months and 1 year LFTs U&Es ECG if clinically indicated (mandatory prior to haloperidol) – see Appendix 9 Prolactin Blood pressure/ pulse baseline and frequently during dose titration then at 12 weeks and 1 year Weight baseline, weekly for 6 weeks (if possible) then at 12 weeks, 6 months and 1 year (plotted on a chart) (olanzapine 3 monthly for first year) Waist circumference (plotted on a chart)	Annual health check* FBC annually Fasting (if possible) blood glucose, HbA _{1c} annually Blood lipid profile - annually LFTs - annually U&Es - annually Prolactin level if signs or symptoms of raised prolactin. See notes overleaf ECG if clinically indicated e.g. high dose, combinations or presence of cardiovascular risk Blood pressure / pulse annually Weight annually (plotted on a chart) Waist circumference annually (plotted on a chart)
Clozapine (Refer to HPFT clozapine policy for more details)	FBC Fasting (if possible) blood glucose / HbA _{1c} at baseline then at 1, 4 - 6 and 12 months Blood lipid profile baseline, then at 3, 4-6 and 12 months LFTs at baseline and then at 4-6 months U&Es baseline ECG baseline Blood pressure and pulse baseline, frequently during dose titration then at 3 months and 12 months Weight at baseline, weekly for 6 weeks (if possible) then at 12 weeks, 6 months and 1 year (plotted on a chart) Waist circumference baseline then at 12 weeks and 1 year (plotted on a chart)	Annual health check* FBC as per monitoring guidelines Fasting (if possible) blood glucose, HbA _{1c} – minimum annually U&Es - annually LFTs – annually Blood lipid profile – annually <i>ECG annually if high dose >600mg/day or otherwise indicated.</i> Blood pressure and pulse – minimum. 6 monthly Weight minimum 6 monthly (plotted on a chart) Waist circumference annually (plotted on a chart)

*Annual Health Check requirements see table 1

ANTIPSYCHOTICS: All antipsychotics are associated with neutropenia, especially in high doses. Cardiovascular mortality is high in patients on antipsychotics, especially those on high doses and combinations. Some antipsychotics are associated with QTc

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prolongation, enhanced by hypokalaemia. Consider an ECG if risk factors are identified for QTc prolongation or arrhythmias (see Appendix 9). Hyperglycaemia and induction of diabetes are associated with atypical antipsychotics. If random or fasting blood glucose is raised an oral glucose tolerance test should be performed. Hyperlipidaemia is common in people on antipsychotics. Hyperprolactinaemia is most likely to be associated with typicals, risperidone and amisulpiride and can lead to sexual dysfunction and menstrual problems.

OLANZAPINE: Weight gain .Transient LFT increase. Significant association with increased lipids, increased glucose and risk of diabetes: Hyperglycaemia is not dose dependent and is reversible on cessation. Can cause hypotension due to action on alpha1 adrenoreceptors

QUETIAPINE: can cause dose related decrease in thyroid hormone levels within 2-4 weeks of initiation that is reversible on stopping the drug. There is no evidence of clinically relevant hypothyroidism. Use with caution and monitor in patients with pre-existing thyroid disease.

CLOZAPINE: Blood dyscrasias: Risk of neutropenia 2.7% and agranulocytosis 0.8%. **Seizures:** Risk increases over 450mg/day. **Raised body temperature** common during initiation but fever should be investigated. Clozapine must be stopped and WBC checked if temperature rises above 38.5° C. Hypersensitivity, **myocarditis** and **cardiomyopathy**. Exacerbation of pre-existing **liver disease**. Impaired glucose tolerance and/or development or exacerbation of diabetes mellitus. As many as a third of patients might develop **diabetes** after 5 years of treatment. Many cases are noted in the first 6 months and some occur within 1 month. Increased risk of **hyperlipidaemia, weight gain, constipation, hypersalivation**. **Gastro-intestinal obstruction:** reactions resembling this reported. Use cautiously with other drugs that cause constipation e.g. antimuscarinics or in history of colonic disease or bowel surgery. Monitor for constipation and prescribed laxative if required.

Appendix 3⁸

Important drug interactions with antipsychotics

Interacting drug or drug class	Effect of interaction	Risk-reduction measures
ACE inhibitors and angiotensin-II receptor antagonists	Increased hypotensive effect	Monitor blood pressure and ask about postural hypotension
Alcohol	Increased sedation	Warn patient of excessive sedation and of psychomotor impairment
Amantadine	Increased risk of extrapyramidal effects	
Amphotericin	Hypokalaemia increases risk of adverse effects of QT-interval prolongation	Ensure any hypokalaemia is corrected
Anaesthetics, general	Increased hypotensive effect	Monitor blood pressure and ask about postural hypotension
Anti-arrhythmics with QT-interval prolonging properties (eg amiodarone, disopyramide, flacainide, and sotalol)	Increased risk of QT-interval prolongation	Preferably avoid concomitant use of drugs that prolong QT interval
Antidepressants, tricyclic	Increased risk of arrhythmias Antimuscarinic effects, especially of phenothiazine antipsychotics, increased	
Antidepressants, tricyclic and SSRIs	Increased risk of seizures	
Citalopram and escitalopram	Increased risk of QT-interval prolongation	Preferably avoid concomitant use of drugs that prolong QT interval
Antiepileptics	Epilepsy control may be impaired	
Antihistamines, sedative	Increased sedation	Select non-sedative antihistamine; warn patient of excessive sedation and of psychomotor impairment
Anxiolytic and hypnotic drugs (eg benzodiazepines)	Increased sedation	Warn patient of excessive sedation and of psychomotor impairment
Atomoxetine	Increased risk of QT-interval prolongation	Preferably avoid concomitant use of drugs that prolong QT interval
Beta-blockers	Increased hypotensive effect	Monitor blood pressure and ask about postural hypotension
Calcium-channel blockers	Increased hypotensive effect	Monitor blood pressure and ask about postural hypotension
Clonidine	Increased hypotensive effect	Monitor blood pressure and ask about postural hypotension
Corticosteroids	Hypokalaemia increases risk of adverse effects of QT-interval prolongation Increased risk of metabolic effects such as weight gain and diabetes	Ensure any hypokalaemia is corrected
Diuretics (loop and thiazide)	Hypokalaemia increases risk of adverse effects of QT-interval prolongation Increased hypotensive effect	Ensure any hypokalaemia is corrected Monitor blood pressure and ask about postural hypotension
Dopamine agonists (eg drugs used for Parkinson's disease)	Antipsychotics inhibit antiparkinsonian effects of dopamine agonists	
Lithium	Increased risk of neuroleptic malignant syndrome, extrapyramidal side effects and CNS toxicity	If concomitant administration necessary, adjust dose so plasma-lithium concentration is at minimum effective level; monitor closely for

		side effects
Methadone	Increased risk of QT-interval prolongation	Preferably avoid concomitant use of drugs that prolong QT interval
Macrolide antibiotics (eg erythromycin, clarithromycin)	Increased risk of QT-interval prolongation	Preferably avoid concomitant use of drugs that prolong QT interval
Metoclopramide	Increased risk of extrapyramidal effects	
Moxifloxacin	Increased risk of QT-interval prolongation	Preferably avoid concomitant use of drugs that prolong QT interval
Opioid analgesics	Increased hypotensive and sedative effect	Monitor blood pressure and ask about postural hypotension; warn patient of excessive sedation and of psychomotor impairment
Tramadol	Increased risk of seizures	