

Factsheet

Antipsychotic Monitoring – 1st and 2nd Generation (Excluding Clozapine)

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FACTSHEET TO FACILITATE PRESCRIBING

PLEASE NOTE THIS IS NOT A SHARED CARE GUIDELINE, NOR IS IT A FULL SUMMARY OF DRUG INFORMATION. ALWAYS REFER TO THE MOST RECENT BNF AND/OR SUMMARY OF PRODUCT CHARACTERISTICS.

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NCL JFC is funded by and provides advice to Acute Trusts and Clinical Commissioning Groups in NCL.

Factsheet – Antipsychotics – 1st and 2nd Generation (excluding clozapine)

Indication information

Refers to individual antipsychotic, 1st and 2nd Generation (excluding clozapine), for licensed indication: schizophrenia and other psychosis, mania, bipolar disorder

Antipsychotic medication is usually initiated by a specialist.

Check list and actions for GP:

1. Ensure documented communication has been received from a specialist including:
 - Indication for use
 - Dose and frequency of medication
 - Duration of treatment
 - Baseline investigations
 - Patient has been counselled on the antipsychotic (including side effects/risks/pregnancy)
2. Before continuation in primary care ensure that the patient meets criteria for continuation of treatment (i.e. antipsychotic treatment is initiated by a specialist and the patient is stabilised on treatment)
3. Conduct necessary blood test monitoring at agreed schedule (see **Clinical Monitoring** section) and communicate results to the mental health team if required
4. Prescribe routine supplies of antipsychotic
5. Monitor the patient's overall physical health and well-being
6. Discuss with a specialist or refer the patient back to the specialist if the patient:
 - Relapses
 - Is intolerant of side effects
 - Is non-compliant with medicines (or this is suspected)
 - Experiences adverse events
 - Has a change in circumstances affecting treatment (e.g. pregnancy)

Note: Clozapine is not included in this factsheet as it is a Red Listed medication not routinely prescribed in primary care

Dose and Administration

Refer to individual manufacturer's [Summary of Product Characteristics \(SPC\)](#) and also current BNF.

For your local formulary please see:

[Camden & Islington Mental Health Trust Formulary](#)

[Barnet, Enfield and Haringey Mental Health formulary](#)

Renal impairment³: No medication clearly preferred to another, however:

Avoid sulpiride and amisulpride as primarily renally excreted

Avoid highly anticholinergic medication because they may cause urinary retention

For further information on renal impairment for specific antipsychotic medication see SPC/BNF.

Hepatic impairment³: Most antipsychotics are hepatically metabolised and may require a dose reduction or be avoided (See **Appendix 1** for choice in specific medication conditions).

Discontinuing treatment³: The decision to stop antipsychotic medication requires a thorough risk-benefit analysis for each patient. Advice should be requested from a specialist. Withdrawal of antipsychotic medication after long-term treatment should be gradual and closely monitored. The relapse rate, in the first 6 months after abrupt withdrawal, is double that seen after gradual withdrawal (defined as slow taper down over at least 3 weeks for oral antipsychotics or abrupt stopping of depot preparations). Abrupt withdrawal may also lead to discontinuation symptoms (e.g. headache, nausea, insomnia) in some patients.

Adverse Effects

If concerned about side effects the [Glasgow antipsychotic side effect scale \(GASS\)](#) is a helpful tool to assess and monitor side effects. Consider referral to a specialist for patients scoring >22 (moderate side effects).

Adverse effects vary between individual antipsychotics.

Significant adverse effects related to antipsychotics⁴: Extrapyramidal side-effects (EPS), Weight gain, Hypertension, Postural hypotension, Sedation, Sexual dysfunction, Hyperprolactinaemia, Impaired glucose tolerance, Dyslipidaemia.

Serious⁴: Psychotropic-related QTc prolongation, Neuroleptic Malignant Syndrome (NMS)

For further information on side effects for specific antipsychotic medication see [SPC/BNF](#). Healthcare professionals are asked to report any suspected adverse reactions using the [Yellow Card Scheme](#).

Contra-indications: Hypersensitivity to the active substance or to any of the excipients.

Special Warnings and Precautions for Use: Antipsychotics can have an influence on the ability to drive and use machines due to potential nervous system and visual effects.

Pregnancy and Breastfeeding⁴: When consideration is given to prescribing psychotropics to any woman of childbearing age, appropriate counselling regarding contraception and the risks of pregnancy (including relapse, risks associated with stopping or changing medication and risk to foetus) should be given. (See **Appendix 1**)

Note: *when switching from medicines known to raise prolactin to one which reduces prolactin a change in fertility can occur which can result in an unplanned pregnancy (see page 7 for details of effect on prolactin).*

Drug Interactions (See Appendix 2)

Please refer to SPC/BNF for full information on interactions with drug name and how to manage these interactions.

Clinical Monitoring

Table 3 Clinical Monitoring⁵

| Frequency Parameter | Baseline | First 6 months of treatment | Annual Check-up | Comments: |
|---|--|--|-----------------|---|
| Glycosylated haemoglobin (HbA1c) | ✓ | ✓ See text 1 | ✓ | Increase frequency if evidence of elevated levels. |
| Blood Lipids (Total cholesterol, non-HDL, HDL, triglycerides) | ✓ | ✓ See text 2 | ✓ | Increase frequency if evidence of elevated levels. Non-fasting samples are satisfactory for most measurements except for triglycerides |
| FBC | ✓ | ✗ | ✓ | Repeat FBC if there are signs and symptoms of a blood dyscrasia |
| LFTs | ✓ | ✗ | ✓ | Repeat LFTs if there are signs of liver toxicity |
| U&Es & Renal Function | ✓ | ✗ | ✓ | |
| TFTs | Baseline and annual check-up only required for patients with bipolar affective disorder & 6 monthly for rapid-cycling bipolar affective disorder. Quetiapine is associated with small (clinically insignificant decreases in thyroid hormones so annual monitoring may be advisable) | | | |
| CPK | ✓ | ✗ | ✗ | Repeat if there are signs and symptoms of NMS |
| Prolactin | ✓ | Consider repeating level 6 - 12 months after initiation. Amisulpride, Risperidone and the Typical Antipsychotics are associated with hyperprolactinaemia. Repeat if there are signs of raised prolactin. | | |
| ECG | ✓ | Where possible offer all patients an annual ECG, especially where other risk factors exist. Baseline ECG for all patients especially if there are specific CV risk factors e.g. high BP. During therapy the need for ECG monitoring should be assessed on an individual patient basis. | | |
| BP & Pulse | ✓ | See comments | ✓ | Monitor BP during titration if there are risk factors for postural hypotension e.g. older adults |
| Weight & BMI | ✓ | ✓ See text 3 | ✓ | |
| Smoking Status | ✓ | ✓ | ✓ | May interact with antipsychotic metabolism |
| Side Effects | ✓ | ✓ | ✓ | If concerned about side effects an optional tool to determine if the patient is suffering from excessive side effects from antipsychotic medication is the Glasgow antipsychotic side effect scale (GASS) |

Where a patient refuses any monitoring an explanation should be given to them of the purpose of monitoring and the risks involved with continuing treatment without monitoring. The decision to continue treatment

without monitoring should be discussed with the patient and specialist. Patients who refuse any monitoring should be reoffered monitoring at regular opportunities.

The clinical Monitoring guidance above should be used in conjunction with the intervention framework ([Lester UK adaptation](#)) for monitoring physical health⁶. If a person has rapid or excessive weight gain, abnormal lipid levels or problems with blood glucose management, consider a referral to a specialist.

1. Glucose and Diabetes monitoring⁵

Increases in glucose occur early on after initiating treatment with antipsychotics and may be difficult to reverse. As changes in glycosylated haemoglobin (HbA1c) occur only after a few weeks, fasting glucose tests should be carried out in preference to HbA1c after treatment initiation. In the long-term blood glucose control can be monitored using HbA1c (as this is more feasible to arrange for patients), however fasting glucose together with HbA1c is preferred at all time-points to determine immediate and long-term impact on blood glucose. Where there is concern about the validity of the HbA1c reading (e.g. in HIV or sickle cell disease) then fasting glucose should always be used. Where a patient also has HIV, discuss concerns about blood glucose levels with their HIV consultant

Monitor fasting glucose and/or HbA1c:

- at 12 weeks,
- at 6 months,
- at 1 year,
- annually thereafter

Increased frequency of testing should be considered for patients at risk of diabetes or where results are high.

Medicines that are High Risk for causing diabetes include **clozapine and olanzapine**.

All patients should be given dietary and lifestyle advice to help prevent the development of diabetes. Management of high glucose should be in line with NICE guidance “type 2 diabetes in adults: management.” <https://www.nice.org.uk/guidance/ng28>

Diabetes UK provides guides on diet and diabetes:

https://shop.diabetes.org.uk/store/managing-your-diabetes/healthcare-professionals/information-for-your-patients/enjoy-food-guides.aspx?_ga=1.66869926.963122193.1465136301

Further diabetes guidelines by NCL JFC can be found at: <http://ncl-mon.nhs.uk/faq/guidelines/>

The [Lester UK adaptation tool](#) for monitoring physical health provides further advice on threshold values used in blood glucose monitoring.

2. **Cholesterol and Lipid monitoring**⁵

Increases in cholesterol and triglycerides can occur after initiating antipsychotics and may continue to increase over the longer term if they are not managed. Increased cholesterol is an established risk factor for cardiovascular disease and intervention to treat dyslipidaemia is known to reduce morbidity and mortality.

Monitor lipids:

- at 12 weeks,
- at 6 months
- at 1 year,
- annually thereafter

Patients with high cholesterol should be given dietary advice and may need treatment in line with NICE guidance on “cardiovascular disease: risk assessment and reduction, including lipid modification”

<https://www.nice.org.uk/guidance/cg181?unlid=737326192016290182>

Patients with diabetes in particular may need aggressive treatment to lower cholesterol.

Further advice on the management of antipsychotic induced dyslipidaemia is available in the British Association of Psychopharmacology guideline on the management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic treatment:

https://www.bap.org.uk/pdfs/BAP_Guidelines-Metabolic.pdf

The NHS provides information on cholesterol including information on how to reduce cholesterol:

<http://www.nhs.uk/Livewell/Healthyhearts/Pages/Cholesterol.aspx>

Further statin prescribing and lipid modification guidelines by NCL JFC can be found at:

<http://ncl-mon.nhs.uk/faq/guidelines/>

The [Lester UK adaptation tool](#) for monitoring physical health provides further advice on threshold values used in blood lipid monitoring.

3. **Weight Gain and Weight monitoring**⁵

Weight gain occurs early on after initiating treatment with antipsychotics and is difficult to reverse. It is therefore important to monitor weight closely during initiation and intervene promptly where weight gain occurs. Patients should be encouraged to weigh themselves and keep a record which can be discussed at each contact.

Monitor weight:

- weekly for the first 6 weeks,
- at 12 weeks,
- at 1 year,
- annually thereafter

Medicines that are High Risk for causing weight gain include **clozapine** and **olanzapine**. **Quetiapine** and **risperidone** have a moderate risk of causing weight gain. Haloperidol has a low risk of causing weight gain and to a low extent.

All patients should be given dietary and lifestyle advice to prevent weight gain. Lifestyle interventions are first line for reversing weight gain.

The NHS provides a range of resources on healthy eating and weight loss. <http://www.nhs.uk/livewell/healthy-eating/Pages/Healthyeating.aspx>

The [Lester UK adaptation tool](#) for monitoring physical health provides further advice on threshold values used in weight monitoring.

Management of abnormal results

QTc prolongation^{3,4}

The QT interval broadly relates to the duration of cardiac repolarisation. Some antipsychotics are linked to prolongation of the cardiac QT interval, a risk factor for the ventricular arrhythmia torsade de pointes, which is often fatal. Overall risk is probably dose-related. Medicine interactions (involving enzyme inhibition) are important (See **Appendix 2** for medication interactions).

See **Appendix 3** for risk factors for QT prolongation.

Table 4: Management of QT prolongation in patients receiving antipsychotic medicines^{3,4}.

| QTc | Action | Refer to cardiologist |
|---|--|------------------------|
| <440msec (men) or <470msec (women) | None unless abnormal T-wave morphology | Consider if in doubt |
| >440msec (men) or > 470msec (women), but < 500msec | Consider referral to specialist to reduce dose or switching to a medicine of lower effect; repeat ECG | Consider |
| >500msec | Repeat ECG. Stop suspected causative medicine(s) and refer to specialist to switch to a medicine of lower effect | Immediately - Same day |
| Abnormal T-wave morphology | Review treatment. Refer to specialist to consider reducing dose or switching to a medicine of lower effect. | Immediately - Same day |
| Correct electrolyte disturbances (potassium and magnesium) if present | | |

Hyperprolactinaemia^{3,4}

Dopamine inhibits prolactin release and so dopamine antagonists can be expected to increase prolactin plasma levels. All antipsychotics cause measurable increases in prolactin but some do not increase prolactin above the normal range at standard doses.

Hyperprolactinaemia is often superficially asymptomatic and there is some evidence that Hyperprolactinaemia does not affect subjective quality of life. Persistent elevated levels of plasma prolactin is associated with sexual dysfunction, reductions in bone mineral density, menstrual disturbances, breast growth, galactorrhoea, suppression of the hypothalamic-pituitary-gonadal axis, and a possible increase in the risk of breast cancer.

| | |
|--|--|
| Antipsychotics that reduce prolactin level | Aripiprazole |
| Antipsychotics that increase prolactin level | Amisulpride, sulpiride, risperidone, paliperidone and first generation antipsychotics |
| Antipsychotics not usually associated with hyperprolactinaemia | Aripiprazole, asenapine, clozapine, lurasidone, olanzapine, quetiapine and ziprasidone |

Table 5: Prolactin concentration interpretation^{3,4}

| | | | |
|--|-------|----------------|------------|
| Normal | Women | 0-25ng/ml | 0-530mIU/L |
| | Men | 0-20ng/ml | 0-424mIU/L |
| Refer to Specialist. Consider a systematic assessment of prolactin-related side effects and discussion of clinical consequences. | | 530 -2500mIU/l | |
| Refer to Specialist. Need referral for tests to rule out prolactinoma. | | >2500mIU/l | |
| Take blood sample at least 1 hour after waking or eating. | | | |
| Minimise stress during venupuncture (stress elevates plasma prolactin). | | | |

Extrapyramidal side effects (EPSE)

Including Dystonia (uncontrolled muscular spasm), Pseudo-parkinsonism (tremor etc.), Akathisia (restlessness), Tardive dyskinesia (abnormal movements) should be considered for a referral to a specialist for a review.

Neuroleptic malignant syndrome (NMS)^{3,4}

Neuroleptic malignant syndrome is a rare, but potentially serious or even fatal adverse effect of all antipsychotics. It is a syndrome of muscular rigidity and sympathetic hyperactivity occurring as a result of dopaminergic antagonism in the context of psychological stressors and genetic predisposition.

Signs and symptoms (Presentation varies considerably): Fever, diaphoresis, rigidity, confusion, fluctuating consciousness, fluctuating blood pressure, tachycardia, elevated creatinine kinase, leucocytosis, altered liver function tests.

Risk factors for NMS:

- high potency first generation antipsychotics
- recent or rapid dose increase
- rapid dose reduction
- abrupt withdrawal of anticholinergics
- antipsychotic polypharmacy
- agitation
- dehydration
- psychosis
- organic brain disease
- alcoholism
- Parkinson's disease
- hyperthyroidism
- psychomotor agitation
- mental retardation

If Neuroleptic malignant syndrome suspected the patient must be sent to A&E

High Dose Antipsychotic Therapy⁴

High dose antipsychotic therapy (HDAT) is defined as a total daily dose of a single antipsychotic which exceeds the upper limit stated in the SPC or BNF with respect to the age of the patient and the indication being treated or a total daily dose of two or more antipsychotics which exceeds the SPC or BNF maximum using the percentage method. The percentage method requires converting the dose of each medicine into a percentage of the BNF maximum recommended dose for that medicine and adding these together (See [Antipsychotic Dosage Ready Reckoner](#)). A cumulative dose of more than 100% is high dose antipsychotic prescribing.

Doses of antipsychotics prescribed above the maximum licensed dosages are off-label. The GP must be informed of the off-label use of the medicine and be willing to accept clinical and legal responsibility for prescribing. The specialist is responsible for ensuring that appropriate information is provided to the GP and the GP agrees to continue the prescription. If the GP does not wish to continue the prescription this needs to be discussed with the specialist recommending treatment.

High doses of antipsychotics might worsen already compromised cognitive function in their patients (particularly older people). High dose antipsychotics have a greater liability for extrapyramidal side effects for which anticholinergic/anti-Parkinsonism medicines might be required which also may worsen cognitive function. Dose-related side effects include extrapyramidal side effects, tachycardia, postural hypotension, sedation, seizures, and hyperprolactinamia.

Additional monitoring will be advised by the specialist. All patients on HDAT should have regular ECGs (baseline, when steady state serum levels have been reached after each dosage increment and then every 6 to 12 months). Additional biochemical/ECG monitoring is advised if medicines that are known to cause electrolyte disturbances or QTc prolongation are subsequently co-prescribed (Appendix 3 Risk factors for QT prolongation)

Contact Details and Further Information:

Camden and Islington NHS Foundation Trust

Mental Health Advice and Assessment Team

Address: 4 St Pancras Way, St Pancras Hospital, London, NW1 0PE, United Kingdom

Phone number: 020 3317 7300

Email: cim-tr.aat-referrals@nhs.net

Opening hours Monday - Friday 9.00am - 5.00pm

Other specialist contact –Crisis Resolution Team: Phone number 020 3317 6333

This number is available 24 hours a day, 7 days a week.

Barnet, Enfield and Haringey Mental Health NHS Trust

Crisis Resolution and Home Treatment Team (CRHT) service

Urgent outreach service, assessing service users 24 hours a day, 7 days a week.

| Borough | Address | Telephone | Fax |
|----------|---------------------------------------|---------------|---------------|
| Barnet | 1st floor, Dennis Scott Unit, Edgware | 0208 702 4040 | 0208 702 4202 |
| Enfield | Ivy House, Chase Farm Hospital | 0208 702 3800 | 0208 702 5062 |
| Haringey | Lea Unit, St. Ann's Hospital | 0208 702 6700 | 0208 442 5890 |

GP Advice Line

An advice line is available for GPs who would like to speak to a consultant about any mental health issue.

Telephone number: 0208 702 3997

Phone line operational Monday - Friday 9am – 5pm

Calls received by 12.45pm will be responded to by a consultant between 1pm and 2pm on the same day. Calls taken after 12.45pm will result in a call back the following day.

<http://www.beh-mht.nhs.uk/gps-and-referrers/>

To find a Summary Product Characteristics: <https://www.medicines.org.uk/emc/>

The [Choice and Medication Website](#) is a patient friendly website which can be provided to patients. Leaflets on medications, including in different languages and formats and fact sheets on a number of areas including weight gain, hyperprolactinaemia, EPSEs and metabolic adverse effects.

[Headmeds](#) is a unique new website about mental health medication for young people aged 13-25. It has been created by YoungMinds and funded by Comic Relief and the Nominet Trust as part of the Innovation Labs project which has developed a range of digital projects to improve young people's mental health.

References

1. Summary of Product Characteristics, <https://www.medicines.org.uk/emc/>
2. BNF 73, March 2017 – September 2017
3. Taylor D. Paton C., Kapur S. Editors. The South London and Maudsley NHS Foundation Trust. Oxleas NHS Foundation Trust. Prescribing Guidelines. 12th Edition. London. Wiley Blackwell (2015).
4. Antipsychotic Prescribing Guideline (PHA35), Camden and Islington NHS Foundation Trust, May 2016
5. Summary of Physical Health Monitoring with Mood Stabilisers & Antipsychotics, Central and North West London NHS Foundation Trust, Updated August 2016 (Version 04.0.0)
6. Positive cardio metabolic health resource, Lester UK Adaptation, 2014 update www.rcpsych.ac.uk/quality/NAS/resources

| Appendix 1: Choice of medication in specific medical conditions^{3,4} | | | |
|--|--|---|---|
| Medical condition | Suggested antipsychotic | Avoid if possible | Comments |
| Epilepsy | Trifluoperazine haloperidol, sulpiride, amisulpride | Clozapine Chlorpromazine (avoid completely) Depot antipsychotics Loxapine (not available in the UK) Lurasidone (experience limited) asenapine (experience limited) Zotepine (avoid completely) (not available in the UK) | Consider referral to specialist and neurologist The majority of antipsychotics decrease the seizure threshold. Clozapine – very epileptogenic. Approximately 5% who receive more than 600mg/day develop seizures. Sodium valproate or lamotrigine are the anticonvulsants of choice as they have a lower incidence of leucopenia than carbamazepine. None of the depot preparations currently available are thought to be epileptogenic. The kinetics of depots are complex (seizures may be delayed). If seizures do occur, the offending medicines may not be easily withdrawn. Depots should be used with extreme care. Beware pharmacokinetic interactions with anticonvulsants (see Appendix 4). |
| Pregnancy | Chlorpromazine (constipation and sedation may occur) Trifluoperazine, Haloperidol, Olanzapine Quetiapine, Clozapine (gestational diabetes may be a problem with all atypical antipsychotics). There is most experience with the above, although safety not fully established | Depot antipsychotics (Anticholinergics) | Consider referral to specialist perinatal services. Discuss with the patient the absolute and relative risks associated with treating and not treating the mental disorder during pregnancy and the postnatal period. If patient established on another antipsychotic, the most up-to-date advice should always be obtained. A change in treatment may not be necessary or wise. |

| Appendix 1: Choice of medication in specific medical conditions ^{3,4} | | | |
|--|---|--|--|
| Breastfeeding | Olanzapine | Clozapine | Consider referral to specialist perinatal services. The benefits of breastfeeding to the mother and infant must be weighed against risk of medicine exposure in the infant. Infant exposure can be decreased by timing feeds to avoid peak medicine levels. |
| Renal impairment | No agent clearly preferred to another. However for typical antipsychotic, suggest haloperidol 2-6mg/day; for atypical agent, suggest olanzapine 5mg/day | Sulpiride Amisulpride Depot antipsychotics Medicines known to prolong QTc interval Highly anticholinergic agents (risk of urinary retention) | Consider referral to specialist. Olanzapine and clozapine may cause or aggravate diabetes, a common cause of renal disease. Avoid medicines known to prolong QTc interval. In established renal failure, electrolyte changes are common so it may be best to avoid antipsychotics with the greatest risk of QTc prolongation. Weight gain (a risk with antipsychotics) may predispose to diabetes which can cause rhabdomyolysis and renal failure. Be vigilant for dystonias and NMS (as the resulting rhabdomyolysis can cause or worsen renal failure). Rhabdomyolysis can occur without symptoms of NMS. |
| Hepatic impairment | Low dose Haloperidol, Sulpiride (no dosage reduction required if renal function is normal) Amisulpride (no dosage reduction required if renal function is normal) Paliperidone: if a depot is required. | Sedative or constipating medicines, e.g. chlorpromazine, clozapine (risk of hepatic encephalopathy). Avoid medications hepatotoxic in their own right e.g. MAOIs, chlorpromazine, clozapine. Avoid medicines with a long-half life or those that need to be metabolised to render them active. Depot antipsychotics. | Consider referral to specialist. Monitor Liver function tests (LFTs) weekly, at least initially. If LFTs deteriorate after a new medicine is introduced, consider switching to another medicine. One third of patients who are prescribed antipsychotics have at least one abnormal LFT and in 4% at least one LFT is elevated three times above the upper limit of normal. Transaminases are mostly affected and this generally occurs within 1-6 weeks of treatment initiation. Only rarely does clinically significant hepatic damage result. |
| Atrial fibrillation | Aripiprazole Lurasidone | Clozapine Olanzapine Paliperidone Avoid QT-prolonging medicines in ischaemic heart disease, and those which increase heart rate. | Consider referral to specialist. In permanent AF with rate control medicine choice is less crucial, but probably best to avoid medicines with potent effects on the ECG (ziprasidone, pimozide, sertindole) and those which increase the heart rate. Avoid QT-prolonging medicines in ischaemic heart disease. |

| Appendix 1: Choice of medication in specific medical conditions ^{3,4} | | | |
|--|--|--|--|
| | | | Beware arrhythmogenicity of psychotropics, their effect on ventricular rate (some induce reflex tachycardia via postural hypotension, others e.g. clozapine, quetiapine directly increase heart rate). Risk of interaction with co-prescribed antiarrhythmics or rate-controlling drugs. |
| HIV | Atypical antipsychotics (risperidone most widely used). Quetiapine, aripiprazole and olanzapine may also be used. | Clozapine not routinely recommended but may be helpful in low doses in patients with higher CD4 counts who are otherwise medically stable. May be helpful in HIV-associated psychosis with medicine-induced parkinsonism. It is not known whether patients with HIV have a greater risk of agranulocytosis, extremely close monitoring of the white cell count is recommended. | Liaise closely with HIV specialists and MDT team. Beware interaction between antipsychotics and antiretrovirals. Idiosyncratic interactions between risperidone and ritonavir have been reported. Patients may be more susceptible to extrapyramidal side-effects, NMS and tardive dyskinesia. |

Appendix 2: Interactions with antipsychotic medication^{3,4}

| Medication | interaction |
|---|---|
| angiotensin converting enzyme (ACE) inhibitors, angiotensin-II receptor antagonists or calcium channel blockers | Postural hypotension |
| Antiarrhythmic medicines | Increased risk of ventricular arrhythmia with anti-arrhythmic medicines that prolong the QT interval such as amiodarone, bretylium, quinidine, sotalol, procainamide, quinidine, disopyramide. |
| Antibacterials | Erythromycin possibly increases plasma concentration of clozapine. Ciprofloxacin can possibly increase the plasma levels of olanzapine. Increased serum levels may result in an increase in seizures. Plasma concentrations of quetiapine are possibly increased by macrolides e.g. erythromycin. The following antibacterials have been associated with QT prolongation and so could have synergistic effect- erythromycin, clarithromycin, ampicillin, co-trimoxazole, pentamidine and some 4-quinolones. |
| Antidepressants | Increased risk of arrhythmia with tricyclic antidepressants. Fluoxetine and venlafaxine increase the plasma concentration of haloperidol. Severe EPSEs have been reported with fluoxetine and haloperidol. |
| Antiepileptics | Carbamazepine lowers the plasma concentration of aripiprazole, chlorpromazine, fluphenazine, haloperidol, olanzapine, paliperidone, quetiapine, risperidone. Phenytoin lowers the plasma concentration of aripiprazole, haloperidol, phenothiazines, quetiapine and risperidone, Phenytoin serum levels are increased by phenothiazines. The risk of neutropenia is increased if clozapine or olanzapine is given with valproate. Valproate possibly increases plasma concentration of quetiapine. Valproate plasma concentration is increased by risperidone. Phenobarbital decreases the plasma concentration of aripiprazole, chlorpromazine, haloperidol, promethazine and quetiapine |
| Antimalarials | The following antimalarials have been associated with QT prolongation and so could have a synergistic effect – chloroquine, mefloquine, quinine. |
| Antivirals | The effect of anti-retrovirals on antipsychotics is unpredictable. 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, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir (reduce dose of aripiprazole). Plasma concentrations of antipsychotics possibly increased by ritonavir. |

| | |
|-----------------|---|
| | <p>There is an increased risk of coma when ritonavir is prescribed concomitantly with risperidone.</p> <p>Lopinavir + ritonavir decrease levels of olanzapine. Use of risperidone decreases the effect of these two antiretrovirals, Can lead to reversible coma and increases propensity for extrapyramidal side effects.</p> <p>Increased risk of ventricular arrhythmias when haloperidol or phenothiazines are given with saquinavir – avoid concomitant use.</p> |
| Atomoxetine | Increased risk of ventricular arrhythmias when antipsychotics that prolong the QT interval are given with atomoxetine. |
| Beta-blockers | Increased risk of ventricular arrhythmias particularly when sotalol is given with zuclopenthixol, haloperidol, amisulpride, phenothiazines and risperidone. |
| Lithium | Increasing lithium levels has a direct neurotoxic effect, including increased risk of neuroleptic malignant syndrome (NMS), particularly with haloperidol and phenothiazines, flupentixol, zuclopenthixol. Possible risk of toxicity when given with olanzapine or sulpiride. |
| Other medicines | The following medicines have been associated with QT prolongation and could have synergistic effect- amantadine, ciclosporin, diphenhydramine, hydroxyzine, nicardipine, tamoxifen. |
| Smoking | Smoking can reduce psychotropic medication effects by enhancing metabolism. Where patients start or stop smoking this may have an impact on their treatment therefore patients should be asked about their smoking status and encouraged to report any changes in their smoking patterns to their team. The use of nicotine replacement therapy does not compensate for this interaction |

Appendix 3: Risk factors for QT prolongation^{3,4}

| Effects of antipsychotics on QTc interval | | |
|--|--|---|
| High effect | A medicine/combination of medicines exceeding the 100% BNF limits | Extensive average QTc prolongation (usually > 20msec at normal clinical doses). |
| Moderate effect | Amisulpride Chlorpromazine Haloperidol Levomepromazine Quetiapine Ziprasidone | Observed to prolong QTc by > 10msec on average when given at normal clinical doses or where ECG monitoring is officially recommended in some circumstances. |
| Low effect | Clozapine Flupentixol Fluphenazine Perphenazine Prochlorperazine Olanzapine Paliperidone Risperidone Sulpiride | Severe QTc prolongation has been reported only following overdose or where only small average increases (<10msec) has been observed at clinical doses. |
| No effect | Aripiprazole | QT prolongation has not been reported either at therapeutic doses or in overdose. |
| Unknown effect | Loxapine Pipothiazine Trifluoperazine Zuclopenthixol | |
| Non-psychotropics associated with QT prolongation | | |
| Antibiotics | Erythromycin, clarithromycin, ampicillin, co-trimoxazole, pentamidine, some 4-quinolones | |
| Antimalarials | Chloroquine, mefloquine, quinine | |
| Antiarrhythmics | Quinidine, disopyramide, procainamide, sotalol, amiodarone, bretylium | |
| Others | Amantadine, cyclosporin, diphenhydramine, hydroxyzine, methadone, nicardipine, tamoxifen | |
| Physiological risk factors | | |
| Cardiac | Long QT syndrome Bradycardia Ischaemic heart disease, Myocardial infarction Myocarditis Left ventricular hypertrophy | |
| Metabolic | Hypokalaemia Hypomagnesaemia Hypocalcaemia | |
| Others | Extreme physical exertion Stress or shock Anorexia nervosa Extremes of age Female gender | |