Prescribing Guidelines
Treatment of Schizophrenia

Scope of this guidance
This guidance aims to describe the pharmacological management of schizophrenia at a simple and intermediate level, with a brief overview of complex or treatment resistant cases. Schizoaffective disorder is not covered.

General Information
- Antipsychotic drug treatment is an essential part of the treatment of schizophrenia.
- Consider likelihood of adequate compliance/concordance before prescribing.
- Preference should also be given to the use of a single antipsychotic. A trial of 6-8 weeks at a therapeutic dose of a particular drug is necessary before concluding that it is ineffective for that patient.
- Polypharmacy of antipsychotics should be avoided except for short periods to cover changeovers. Patients would require close monitoring of physical health as polypharmacy leads to higher incidence of side effects. Refer to the ABHB protocol on High Dose/ Multiple Antipsychotics.
- All patients on antipsychotics should undergo regular physical health monitoring.
- NICE guidance is available: Schizophrenia Introduction CG82

Choice of Drug
- Typical antipsychotics appear to be just as effective as atypical antipsychotics (with the exception of clozapine).
- Typical antipsychotics are associated with high risk of movement disorder, particularly tardive dyskinesia (TD) and atypical antipsychotics are associated with a higher risk of metabolic syndrome.
- Choice is based on comparative side-effects, relative toxicity, and whether first or second line use

First line drugs for First Episode Psychosis
- Based on side effect profile and cost-effectiveness it is recommended that risperdone should be considered first line in the management of 1st episode psychosis.
- Consider cross tapering to a 2nd line drug if risperdone remains ineffective after 4 weeks.
- Clozapine must not be used as a 1st line drug.
- Only use Quetiapine XL if the IR has been tried and is not tolerated, or is affecting compliance.

Maintenance treatment for Schizophrenia
- Continue medication based on response in the acute episode.
- Monitor and respond to side effects and adverse eventsPatients should receive an annual health promotion and prevention review and advice appropriate to their age, gender and health status. Primary Care’s Quality and Outcomes Framework (QOF) includes 6 physical health indicators within the mental health domain: Blood pressure (MH003); total cholesterol to HDL ratio (MH004); blood glucose or HbA1c (MH005); BMI (MH006); alcohol consumption record (MH007) and a previous cervical screening test in the period specified in national recommendations (MH008). See Appendix Three
- Healthcare professionals in secondary care should ensure that the regular physical health checks are being carried out in primary care.
- Monitor compliance. Consider using a standardised assessment to support this, e.g. Symplex Information Solutions – Solutions – Lunsers/eLunsers

Relapse of Schizophrenia
- Optimise existing treatment.
- Assess compliance.
- Exclude co morbidity.
- Restart effective treatment based on above notes.
- Consider depot antipsychotic injection if compliance with oral medication remains poor.

NB: Depot antipsychotic medication including typical antipsychotics should be considered at any time if compliance is an issue or if a preference for this is expressed by the patient.
### ATYPICAL ORAL ANTIPSYCHOTICS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Cost rating Jul 13 (£)</th>
<th>Dose Regime</th>
</tr>
</thead>
</table>
| Risperidone | - Little sedation  
- Low incidence of extra-pyramidal side effects (EPSE) in doses of 6 mg or less                                                                                                               | - Raised serum prolactin levels  
- First dose hypotension - titrate dose.  
- Weight gain  
- Nausea, dyspepsia, abdominal pain  
- Mild anti-cholinergic effect                                                                                                                   | £14 per year       | Usual Daily Dose 4mg |
| Olanzapine  | - Minimal effect on serum prolactin  
- Lower incidence of sexual dysfunction.  
- Less hypotensive  
- Generally well-tolerated                                                                                                                       | - More sedating (could be desirable in some cases)  
- Significant weight gain - monitor frequently for 3 months, then 3 monthly for the first year, then yearly  
- High incidence of lipid abnormalities - monitor baseline, 3 monthly for the first year, then yearly  
- Diabetes - Monitor blood glucose at baseline, 1 month and then 4-6 monthly                                                                 | £33 per year       | Usual Daily Dose 15mg |
| Quetiapine  | - Generally well-tolerated  
- No EPSE  
- No effect on serum prolactin                                                                                                                                                                         | - More sedating (could be desirable in some cases)  
- First dose hypotension - titrate dose  
- Weight gain  
- QT prolongation  
- Elevated plasma lipids                                                                                                                          | £78 per year       | IR tablets Usual daily dose 600mg |
|             |                                                                                                                                                                                                           |                                                                                                                                                                                                                                   |                        | XL tablets Usual daily dose 600mg |
|             |                                                                                                                                                                                                           |                                                                                                                                                                                                                                   |                        | £2000 per year |
| Amisulpiride| - Little sedation  
- Lower incidence of weight gain  
- No hypotension  
- Little or no anti-cholinergic effect  
- Renal excretion                                                                                                                                  | - High incidence of raised prolactin levels                                                                                                                                         | £710 per year       | Usual daily dose 400mg |
| Aripiprazole| - Little effect on serum prolactin and QT prolongation  
- Low incidence of weight gain, glucose intolerance                                                                                                                                                   | - May cause anxiety if given at full dose on initiation  
- May cause EPSE                                                                                                                                                                                                                     | £1,250 per year      | Usual daily dose 15mg |

**Other Atypicals**  
Sertindole (named patient only), Zotepine, Paliperidone (oral form non formulary)

### TYPICAL ORAL ANTIPSYCHOTICS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Dose Regime</th>
</tr>
</thead>
</table>
| Haloperidol                   | - Lower rates of sedation, weight gain, anti-cholinergic effects & hypotension compared to other typicals                                                                                                  | - High prevalence of EPSE  
- Raised serum prolactin  
- Weight gain  
- ECG abnormalities - baseline ECG & after dose changes                                                                                                                          | Initially 3-5 mg bd/tid daily, then titrate dose according to response  
Max: 30mg daily                          |
| Trifluoperazine               | - Less sedating compared to other phenothiazines                                                                                                                                                       | - High prevalence of EPSE  
- Raised serum prolactin  
- Weight gain                                                                                                            | Initially 5 mg bd increase by 5 mg after 1 week, then at interval of 3 days according to response              |
| Zuclopenthixol Dihydrochloride| - Less hypotensive  
- May be more effective in agitated/aggressive patients                                                                                                                                              | - Raised prolactin levels  
- EPSE  
- Weight gain  
- Sedation  
- Anti-cholinergic effect                                                                                                                                       | Initially 20-30 mg in divided doses  
Usual maintenance: 20-50mg daily.  
Max: 150mg daily                                |
| Flupenthixol                  | - Less sedating  
- Less hypotensive                                                                                                                                                                                  | - EPSE  
- Weight gain  
- Raised prolactin levels  
- Antidepressant effect (not proven)                                                                                                                                         | Initially 3-9mg twice daily adjusted according to response  
Max 18 mg daily                          |
| Sulpiride                     | - Less EPSE  
- Less hypotensive  
- Low prevalence of weight gain                                                                                                                                                                         | - Marked increase in serum prolactin levels  
- Some sedation                                                                                                         | 200-400 mg BD  
Max: 2400 mg daily |
| Pimozide                      | - Less sedating  
- Less weight gain  
- Less EPSE                                                                                                                                                                                          | - QTc prolongation - baseline ECG and after dose changes  
- Raised serum prolactin levels                                                                                                                                            | Initially 2 mg OD, increase gradually at weekly intervals by 2-4mg  
Max: 20 mg daily                          |
| Chlorpromazine, Levomepromazine, Pericyazine, Perphenazine | - High incidence of side effects  
- Rarely used - better alternatives available                                                                                                                                                     | Please refer to BNF section 4.2                                                                                                                                             |                                                                                                                                 |

Author: Juliet Shepherd  
Clinical Pharmacist, Mental Health  
(Paliperidone guidelines adapted from the South Staffordshire and Shropshire NHSFT prescribing guidelines)
### TYPICAL DEPOT ANTI PSYCHOTICS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Dose Regime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol depot</td>
<td>• See above</td>
<td>• See above</td>
<td>• Initially 50mg IM four weekly&lt;br&gt;• Increase if necessary by 50mg increments to 300mg four weekly</td>
</tr>
<tr>
<td>Zuclopenthixol Decanoate</td>
<td>• See above</td>
<td>• See above</td>
<td>• Test dose: 100mg IM, then 200-500mg at least 7 days later.&lt;br&gt;• Repeat at intervals of 1-4 weeks&lt;br&gt;• Max: 600mg weekly</td>
</tr>
<tr>
<td>Flupenthixol Decanoate</td>
<td>• See above</td>
<td>• See above</td>
<td>• Test dose: 20mg IM, then after at least 7 days by 20-40mg&lt;br&gt;• Repeat at intervals of 2-4 weeks&lt;br&gt;• Usual maintenance: 50mg every four weeks to 300mg every two weeks.&lt;br&gt;• Max: 400mg weekly</td>
</tr>
<tr>
<td>Fluphenazine Decanoate</td>
<td>• See above</td>
<td>• See above</td>
<td>• Test dose: 12.5mg IM, then after 4-7 days 12.5-100mg repeated at intervals of 14-35 days</td>
</tr>
<tr>
<td>Pipotiazine Palmitate</td>
<td>• Weight gain&lt;br&gt;• EPSE&lt;br&gt;• Raised serum prolactin&lt;br&gt;• Sedation&lt;br&gt;• Hypotension</td>
<td>• Test dose: 25mg IM, then 25-50 mg after 4-7 days&lt;br&gt;• Usual maintenance 50-100mg four weekly.&lt;br&gt;• Max: 200mg</td>
<td></td>
</tr>
</tbody>
</table>

### ATYPICAL DEPOT ANTI PSYCHOTICS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone LAI (Risperdal Consta)</td>
<td>• Not for first line use – only after typical depots have failed/not tolerated&lt;br&gt;• See attached guideline in Appendix One</td>
</tr>
<tr>
<td>Paliperidone LAI (Xeplion)</td>
<td>• Seek approval from Dr Chance before starting therapy&lt;br&gt;• See All Wales Medicines Strategy Group (AWMSG) for recommendation details AWMSG Recommendations&lt;br&gt;• See attached guideline in Appendix Two</td>
</tr>
</tbody>
</table>

### TREATMENT-RESISTANT SCHIZOPHRENIA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>Refer to Clozapine care pathway on the ABHB intranet&lt;br&gt;<a href="http://example.com">Aneurin Bevan Health Board Medicines &amp; Therapeutics Committee - Mental Health Prescribing Guidelines &amp; Resources</a></td>
</tr>
</tbody>
</table>
Appendix One

Guidelines for Establishing patients on Risperidone long acting injection (Risperdal® Consta™)

Dosing

- Recommended starting dose is 25mg by deep intramuscular injection every two weeks
- For patients established on oral risperidone >4mg/day then consider 37.5mg every 2 weeks
- Maximum dose should not exceed 50mg every 2 weeks
- Patients with no previous history of taking risperidone should be pre-treated with oral risperidone for several days where clinically feasible, to assess tolerability before the first injection

Dose Adjustments

- Oral risperidone 1 – 4mg/day can be temporarily added to treatment while establishing patients on the optimal dose
- If extended periods of oral supplementation are required then consider increasing the dose of Risperdal Consta
- Consider adjusting the dose of Risperdal Consta only after a minimum of 4 weeks from the previous dose adjustment
- See Table One

Points to Consider

- A minimum of 3 weeks antipsychotic cover is required after the first injection of Risperdal Consta until the main release phase of risperidone begins
- Some patients may require additional antipsychotic cover for longer – the dose should be adjusted according to the patient’s clinical response
- Steady state plasma levels of risperidone are typically achieved after four consecutive injections of Risperdal Consta (after initiation or after any dose increase)
- Some patients may start to see symptom improvement after one month, though further improvement is seen over 3 – 6 months and is continued in the long term

Switching from oral antipsychotics to Risperdal Consta

- Patients not stabilised on oral Risperdal should be provided with cover during a minimum of the first 3 weeks after the first injection with Risperdal Consta, until the main release phase of risperidone from the injection site has begun
- Taper the previous oral antipsychotic after a minimum of the first 3 weeks according to the patient’s symptoms, level of side effects, and risk for relapse; abrupt medication discontinuation is not recommended.

Switching from depot antipsychotics to Risperdal Consta

- Patients not stabilised on oral Risperdal should have cover during a minimum of the first 3 weeks after the first injection with Risperdal Consta, until the main release phase of risperidone from the injection site has begun.
- Give the Risperdal Consta injection the week before the last depot injection is due
  Or: Give the Risperdal Consta injection instead of the last depot injection (on its due date), and supplement with oral Risperdal for the first 3 weeks.
- Depending on the frequency with which the depot was given, ensure that any necessary supplementation during the first 3 weeks is with oral risperidone at an appropriate dose.
### Establishing patients on risperidone long acting injection (Risperdal® Consta™)

<table>
<thead>
<tr>
<th>START</th>
<th>After WEEK 1</th>
<th>After WEEK 2</th>
<th>After WEEK 3</th>
<th>After WEEK 4</th>
<th>After WEEK 5</th>
<th>After WEEK 6</th>
<th>After WEEK 7</th>
<th>After WEEK 8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risperdal® Consta™</strong></td>
<td></td>
<td></td>
<td></td>
<td>After a minimum of 4 weeks, a change can be considered from 25mg to 37.5mg</td>
<td></td>
<td></td>
<td></td>
<td>Dose increase can be considered. Maximum dose 50mg</td>
</tr>
<tr>
<td>25mg</td>
<td></td>
<td></td>
<td>NO DOSE CHANGE</td>
<td></td>
<td></td>
<td>NO DOSE CHANGE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37.5mg</td>
<td></td>
<td>NO DOSE CHANGE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Oral antipsychotic**

**ORAL ANTIPSYCHOTIC SUPPLEMENTATION**

Assess need for oral antipsychotic supplementation

**ORAL ANTIPSYCHOTIC SUPPLEMENTATION** AS REQUIRED

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*If switching from depot antipsychotic: patient should receive first injection of Risperdal Consta on the due date of their next depot antipsychotic. During first three weeks of Risperdal Consta consideration should be given to supplementation with oral risperidone.*
Guidelines for Establishing Patients on Paliperidone Long-Acting Injection

The Mental Health Medicines Management Group requires that an intention to prescribe is made by email to Dr Patrick Chance. Spending on Paliperidone in ABHB will be monitored to ensure that the guidelines are being followed.

Indications
Paliperidone Long Acting Injection (PLAI) is indicated for maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. PLAI may be an effective treatment option in patients who have shown an initial treatment response to paliperidone or risperidone but for whom concordance with oral medication is a problem. (Reflecting the 2009 NICE guidance, PLAI should be offered as a treatment option alongside other long acting antipsychotic injections (depos)). Please note that oral paliperidone is non formulary in ABHB.

The following table outlines actions that should be followed in different situations where Paliperidone long acting injection may be considered.

<table>
<thead>
<tr>
<th>Status</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patient concordant with oral antipsychotics</td>
<td>Continue oral antipsychotics</td>
</tr>
<tr>
<td>2. Patient stabilised on an oral antipsychotic for at least two weeks but there are compliance issues</td>
<td>Offer choice of long acting injection or typical depot.</td>
</tr>
<tr>
<td>3. Initial dose, when transferring from oral antipsychotic therapy</td>
<td>Recommended initiation is with a dose of 150mg on treatment day 1 and 100mg one week later (i.e. day 8) both administered in a deltoid muscle. The recommended monthly maintenance dose is 75mg; with individual patients’ doses tailored within the range of 25mg to 150mg based on tolerability and/or efficacy. Further doses can be administered into deltoid or gluteal muscle. Previous oral paliperidone or oral risperidone regardless of the previous dose can be discontinued at the time of first administration of paliperidone.</td>
</tr>
<tr>
<td>4. Elderly (&gt;65 years).</td>
<td>Not recommended – Off Label</td>
</tr>
<tr>
<td>5. Maintenance Treatment and Dose Changes. Monthly dosing is by calendar month, not 4 weekly. Administering 4 weekly will cost more per year. Following the second dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle. Dose changes can be made on a monthly basis, after the second dose, based on tolerability and efficacy with the maintenance dose range being between 25mg to 150mg. 150mg per month is approximately £5000 per patient per year and should only be considered in extreme circumstances.</td>
<td></td>
</tr>
<tr>
<td>6. Switching from Risperidone Long Acting Injection</td>
<td>Initiate paliperidone LAI in place of the next scheduled injection of risperidone LAI (deltoid or gluteal). For equivalent doses please see Table 1 below. Paliperidone LAI should then be administered at monthly intervals. The one week initiation regimen (Day 1 and Day 8 respectively) is not required.</td>
</tr>
<tr>
<td>7. Patient stabilised on an older long acting antipsychotic injection but experiencing unacceptable side effects or it has not been sufficiently effective</td>
<td>Provided the patients has shown a previous responsiveness to either oral risperidone or paliperidone commence paliperidone on the day that the next depot injection is due (Day 1) in deltoid muscle but do not administer the second initiation dose on Day 8. Administer subsequent doses on a monthly basis based on clinical assessment – see point 5 for dose regimens.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 1 Previous Risperidone LAI Dose</th>
<th>Paliperidone LAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>25mg every 2 weeks</td>
<td>50mg monthly</td>
</tr>
<tr>
<td>37.5mg every 2 weeks</td>
<td>75mg monthly</td>
</tr>
<tr>
<td>50mg every 2 weeks</td>
<td>100mg monthly</td>
</tr>
</tbody>
</table>

Further information on administration can be found on the Medicines and Therapeutics Committee Website

Aneurin Bevan Health Board Medicines & Therapeutics Committee
Positive Cardiometabolic Health Resource | An intervention framework for patients with psychosis on antipsychotic medication

**Smoking**
- **Current smoker**
  - Brief individual intervention
  - Consider referral to NHS Smoking cessation programme
  - Consider nicotine replacement therapy

**Lifestyle**
- **Poor diet AND/OR Sedentary lifestyle**
  - Target: Improve quality of diet
  - Target: Daily exercise of 30mins/day

**BMI**
- **BMI ≥ 25 kg/m²**
  - Target: BMI 18.5 – 24.9 kg/m²
  - Target: BMI 18.5 – 22.9 kg/m² if South Asian or Chinese

**Blood Pressure**
- **>140 mm Hg systolic AND/OR >90 mm Hg diastolic**
  - Target: <140/90 mm Hg
  - Target: <140/80 mm Hg for those with CHD

**Glucose Regulation**
- **HbA1C or Glucose threshold**
  - Target: HbA1C 59 mmol/mol
  - Target: HbA1C 59 mmol/mol OR other higher level agreed with the individual

**Blood Lipids**
- **Total chol ≥ 6.0 mmol/l OR High (>20%) risk of CVD**
  - Target: Total chol ≤ 5.0 mmol/l

**Lifestyle advice to include diet and physical activity.**

**Medication review**

Refer for investigation, diagnosis and treatment by appropriate clinician if necessary:
- **Smoking**
- **Lifestyle**
- **BMI**
- **Blood Pressure**
- **Glucose Regulation**
- **Blood Lipids**

**FPG** = Fasting Plasma Glucose | **BMI** = Body Mass Index | **Total Chol** = Total Cholesterol | **LDL** = Low Density Lipoprotein | **HDL** = High Density Lipoprotein
## History and examination following initiation or change of antipsychotic medication

**Frequency:** as a minimum review those prescribed a new antipsychotic at baseline and at least once after 3 months. Ideally weight should be assessed 1-2 weekly in the first 8 weeks of taking a new antipsychotic as rapid early weight gain may predict severe weight gain in the longer term. Subsequent review should take place annually unless an abnormality of physical health emerges, which should then prompt appropriate action and/or continuing review at least every 3 months.

**At review**

**History:** Seek history of substantial weight gain (e.g. 5kg) and particularly where this has been rapid (e.g. within 3 months). Also review smoking, exercise and diet. Ask about family history (diabetes, obesity, CVD in first degree relatives <60 yrs) and gestational diabetes. Note ethnicity.

**Examination:** Weight, BMI, BP.

**Investigations:** Fasting estimates of plasma glucose (FPG), HbA\textsubscript{1c}, and lipids (total cholesterol, LDL, HDL, triglycerides). If fasting samples are impractical then non-fasting samples are satisfactory for most measurements except for LDL or triglycerides.

**ECG:** Include if history of CVD, family history of CVD, or if patient taking certain antipsychotics (see Summary of Product Characteristics) or other drugs known to cause ECG abnormalities (eg erythromycin, tricyclic anti-depressants, anti-arrythmics – see British National Formulary for further information).

## Interventions

**Nutritional counselling:** reduce take away and “junk” food, reduce energy intake to prevent weight gain, stop soft drinks and juices, increase fibre intake.

**Physical activity:** structured education-lifestyle intervention. Advise physical activity: e.g. Advise a minimum of 150 minutes of ‘moderate-intensity’ physical activity per week ([http://bit.ly/0e7DeS](http://bit.ly/0e7DeS)).

If unsuccessful after 3 months in reaching targets, then consider specific pharmacological interventions (see below).

### Specific Pharmacological Interventions


• Where intensive lifestyle intervention has failed consider metformin trial (this would normally be GP supervised).

• Please be advised that off-label use requires documented informed consent as described in the GMC guidelines, [http://www.gmc-uk.org/static/documents/content/Good_Practice_in_Prescribing_Medicines_0911.pdf](http://www.gmc-uk.org/static/documents/content/Good_Practice_in_Prescribing_Medicines_0911.pdf). These GMC guidelines are recommended by the MPS and MDU, and the use of metformin in this context has been agreed as a relevant example by the Defence Unions.

• Adhere to BNF guidance on safe use (in particular ensure renal function is adequate). Start with a low dose e.g 500 mg once daily and build up, as tolerated, to 1500–2000 mg daily.

**Review of antipsychotic medication:** Normally psychiatrist supervised. Should be a priority if there is:

• Rapid weight gain (e.g. 5kg <3 months) following antipsychotic initiation.

• Rapid development (<3 months) of abnormal lipids, BP, or glucose.

The psychiatrist should consider whether the antipsychotic drug regimen has played a causative role in these abnormalities and, if so, whether an alternative regimen could be expected to offer less adverse effect:

• As a first step prescribed dosages should follow BNF recommendations; rationalise any polypharmacy.

• Changing antipsychotic requires careful clinical judgment to weigh benefits against risk of relapse of the psychosis.

• Benefit from changing antipsychotic for those on the drug for a long time (>1 year) is likely to be minimal.

• If clinical judgment and patient preference support continuing with the same treatment then ensure appropriate further monitoring and clinical considerations.