Psychosis and schizophrenia represent major psychiatric disorders in which a person’s perceptions, thoughts, mood and behaviour are significantly altered. Typically, there is a ‘prodromal’ period often characterised by deterioration in personal functioning followed by an acute phase marked by positive symptoms and subsequently negative symptoms that can have a considerable effect on personal, social and occupational function. Affective dysfunction, comorbidities and poor physical health are highly prevalent in people with psychosis and schizophrenia.

In the management of schizophrenia, antipsychotics may be used for the treatment of acute episodes or recurrence of psychosis, long-term relapse prevention, emergency treatment of acute behavioural disturbance and symptom reduction. Antipsychotics are also used in combination with a range of other classes of medication including anticonvulsants, mood stabilisers, anticholinergics, antidepressants and benzodiazepines as augmentation strategies where there is a lack of effective response to antipsychotics alone, for behavioural control, for the treatment of the side effects of antipsychotics and for the treatment of comorbid or secondary psychiatric problems, such as depression and anxiety.

Prescribing and Use of Antipsychotics

- An oral antipsychotic in conjunction with a psychological intervention (family intervention and individual cognitive behavioural therapy (CBT) is recommended by NICE guidelines for treatment of first episode psychosis or for treatment of acute exacerbation or recurrence of psychosis or schizophrenia.
- For people with an acute exacerbation or recurrence of psychosis or schizophrenia, review existing medication and optimise the dose.
- The choice of antipsychotic should be determined by the service user’s current symptoms, previous clinical response and side effects, past medication history, comorbidities, concurrent treatments and individual preferences (including advance statements, advance decisions about treatment and carer views, if appropriate). See Appendix 1.
- Discuss the condition, benefits and side-effects of each drug with the service user and/or carer and provide appropriate written information.
- Check and discuss the effects and potential interactions of prescribed medications with non-prescribed and complementary therapies, alcohol, smoking and illicit drugs.
- For people with coexisting substance misuse, assess the level and type of substance misuse, interactions and increased risk of side effects and offer any appropriate interventions.
- Undertake and record relevant baseline investigations and routine monitoring.
- Initiate treatment at the lower end of the licensed dose range and slowly titrate upwards within the recommended dose range to allow monitoring for the early emergence of side effects, weight gain or insomnia. Be aware that antipsychotic-naive individuals may respond to doses of antipsychotics at the lower end of the recommended range.
- Carry out a therapeutic trial of oral antipsychotics at the optimum dosage for 4–6 weeks.
- To reduce risk of relapse, antipsychotic treatment should be continued for at least 1–2 years after the person has recovered and remained stable.
- Prescribe antipsychotics within the recommended dose range as there is little evidence to support benefits of higher dosage. If high-dose antipsychotic treatment is initiated, use for a limited therapeutic trial and return to normal after a 3-month period unless the clinical benefits clearly outweigh the risks. Provide a clear rationale to the service user, document and monitor.
Prescribing and Use of Antipsychotics continued

- Do not routinely initiate regular combined antipsychotic medication, except for short periods (for example, when changing medication) because this results in prescribing higher than necessary total dosage and increases the risk of side effects.
- Do not use loading doses or intermittent dose maintenance strategies routinely.
- Consider depot/long-acting injectable antipsychotic medication for maintenance treatment of people with schizophrenia who would prefer such treatment after an acute episode or where clinically indicated to avoid covert non-adherence (see Appendix 1) Where possible, long-acting injectable antipsychotics without prior stabilisation on oral treatment should not be used in treatment-naïve or in acutely disturbed service users.
- Consider clozapine for treatment resistant illness, i.e. following inadequate response to treatment despite optimal use of at least two different antipsychotic drugs (including at least one second generation antipsychotic). People taking clozapine must be registered with a clozapine monitoring service and are subject to mandatory monitoring of full blood counts.
- Review PRN use of antipsychotics regularly, e.g. weekly or as appropriate and be aware that PRN prescriptions may lead to doses above the maximum licensed range.
- Review and record the effects of antipsychotic medication annually, including response to treatment, side effects, movement disorders, weight and other physical health parameters for at least 12 months before transferring responsibility to primary care. Antipsychotics should not be prescribed for people considered at risk of psychosis with the aim of reducing risk or preventing psychosis. Such people should be monitored and managed with psychological therapies e.g. CBT and/or family intervention.
- If withdrawing antipsychotic medication, undertake gradually and monitor regularly for signs and symptoms of relapse. After withdrawal from antipsychotic medication, continue monitoring for signs and symptoms of relapse for at least 2 years.

Side Effects and Interactions

- Antipsychotics can be divided into older first-generation ('FGAs', 'conventional' or 'typical') and newer second-generation ('SGAs' or 'atypical') antipsychotics.
- All are associated with a high incidence and broad range of side effects. The risk varies with the type of antipsychotic (first-generation or second-generation), the individual drug and the person.
- In general, second-generation antipsychotics are associated with fewer extrapyramidal side effects than first-generation antipsychotics. However, second-generation antipsychotics are associated with several other important adverse effects, such as weight gain and metabolic effects (e.g. glucose intolerance, hyperlipidaemia, hyperprolactinaemia)
- Adverse effects of antipsychotics include extrapyramidal symptoms (dystonic reactions, akathisia, tardive dyskinesia); gastrointestinal effects (including constipation, dry mouth, nausea, vomiting and dyspepsia), sedation; postural hypotension; hypertension; anticholinergic effects (such as dry mouth, blurred vision, raised intra-ocular pressure urinary retention, constipation); weight gain; dyslipidaemia; hyperprolactinaemia; sexual dysfunction, impaired glucose tolerance; QT interval prolongation; blood dyscrasias; reduced seizure threshold; venous thromboembolism (VTE); abnormal liver function tests (LFTs) and photosensitivity
- Less frequent but serious adverse effects include neuroleptic malignant syndrome, seizures, serious ventricular arrhythmias and sudden cardiac death.
- Older adults are particularly prone to the side effects of antipsychotics. The balance of risks and benefit should be carefully considered before prescribing.
- Important drug interactions commonly occur between antipsychotics and other drugs that interfere with hepatic enzymes; cause CNS depression (e.g. alcohol, benzodiazepines, opioids) OR increase the risk of arrhythmias (e.g. diuretics); cause QT-interval prolongation; lower blood pressure and cause hypotension; lower seizure threshold or cause other neurotoxicities. Due to their mode of action (blocking dopamine-2 receptors), antipsychotics inhibit the effect of dopamine agonists used for Parkinson's disease.
Precautions and Safety Warnings

- There is a clear increased risk of stroke and a small increased risk of death associated with use of both typical and atypical antipsychotics in older adults with dementia and in any person with pre-existing risk factors for stroke. The possibility of cerebrovascular events should be considered carefully before treating people with a history of stroke or transient ischaemic attack or risk factors for cerebrovascular disease.
- Antipsychotic use may be associated with an increased risk of venous thromboembolism (VTE). All possible risk factors for VTE should be identified before and during antipsychotic treatment and preventive measures undertaken.
- Antipsychotic lower seizures threshold in a dose-related manner. Use with caution in epilepsy.
- Neuroleptic malignant syndrome (NMS), a rare but life-threatening adverse effect, can occur with any antipsychotic and is a medical emergency requiring immediate discontinuation of the antipsychotic. Symptoms include hyperthermia, muscle rigidity, autonomic instability and fluctuating consciousness. NMS is a medical emergency and requires immediate management.
- QT interval prolongation is a widely reported class side effect of antipsychotics. It increases the risk of serious arrhythmias such as torsades de pointes. ECG monitoring may be necessary.
- Antipsychotic drugs can cause sedation, poor concentration, and extrapyramidal symptoms, all of which can impair driving. Careful assessment is therefore needed to determine whether adverse effects of medication will impair driving.
- The use of antipsychotics in the treatment of psychosis in patients with Parkinson's disease is not routinely recommended.
- Routine blood monitoring is a mandatory pre-requisite to clozapine use because of the risk of neutropenia and agranulocytosis. Ongoing monitoring must be maintained.
- When discontinuing antipsychotic, reduce the dose gradually and monitor for withdrawal reactions and signs of symptoms of relapse. After withdrawal of antipsychotic medication, continue monitoring for signs and symptoms of relapse for at least 2 years.
- Smoking induces the metabolism of psychotropic medication (particularly olanzapine and clozapine). Dose adjustments may be necessary on smoking cessation or reduction.

Monitoring and Management of Physical Health

- The physical health of service users treated with antipsychotic should be assessed, documented, monitored and appropriate interventions offered, where appropriate.
- A combined healthy eating and physical activity programme should be offered.
- Smoking status and other lifestyle parameters (including diet, exercise, alcohol and substance misuse) should be assessed and appropriate interventions offered. Smokers should be offered help and treatment for smoking reduction or cessation with medication adjusted as appropriate.
- Before starting antipsychotic medication, baseline physical health checks should be carried out including weight/body mass index, waist circumference, nutritional status, diet, level of physical activity, sexual health, blood pressure/pulse, urea and electrolytes/renal function, liver function tests, full blood counts, fasting glucose, glycosylated haemoglobin (HbA1c), blood lipid profile, prolactin levels and movement disorders.
- NICE states that an electrocardiogram (ECG) is required before starting antipsychotic medication and periodically thereafter, if specified by the product licence, or if there is history or risk of cardiovascular disease, or if the service user is being admitted as an inpatient.
- During treatment, weight should be measured weekly for the first 6 weeks, then at 12 weeks, at 12 months and then annually (plotted on a chart) and waist circumference annually (plotted on a chart); pulse and blood pressure at 12 weeks, at 12 months and then annually; fasting blood glucose, HbA1c and blood lipid levels at 12 weeks, at 12 months and then annually thereafter.
- People with rapid or excessive weight gain, abnormal lipid or blood glucose levels, and smokers should be identified and managed in line with relevant NICE guidance.
- Results of all monitoring should be documented in the case notes and communicated to the GP.
- Monitor physical health for at least 12 months or until the service user’s condition has stabilised before transferring responsibility to primary care. Review antipsychotic medication annually.

Mersey Care Clinical Guideline / Formulary Document

Psychosis and Schizophrenia

Updated: Jan 2017
Next Review: Jan 2019
Treatment Resistant Schizophrenia

- Review the diagnosis.
- Check adherence to treatment, dose and duration of treatment.
- Consider and offer a psychological intervention e.g. CBT.
- Consider other cause of non-response e.g. alcohol and substance misuse, medication, or physical illness.
- Clozapine has evidence of superior efficacy in people whose symptoms have not responded to adequate doses of at least two different antipsychotics, one of which is a second-generation antipsychotic.
- If there is an inadequate response to clozapine at optimal dose or poor tolerability, augmentation with an antipsychotic or other psychotropic agents may be beneficial. An adequate trial of clozapine augmentation may be up to 8–10 weeks. Choose a drug that does not compound the common side effects of clozapine.
- If clozapine augmentation is unsuccessful, consider switching to another antipsychotic, although evidence of efficacy is not consistent.
- Consider augmentation of antipsychotic with other drugs like lithium, carbamazepine, sodium valproate, lamotrigine, antidepressants and benzodiazepine.
- Use of high-dose antipsychotic medication and combinations of antipsychotics is common, but there is little evidence of any significant benefit and side effects are greater. Routine use is not recommended.

Behavioural Disturbance

- For acute severe behavioural disturbance requiring rapid tranquillisation, follow Trust Policy and recommendations in the Violence, Aggression and Severe Behavioural Disturbance clinical guideline document.

Further Information

- Full guidance on prescribing and use, including information on possible side effects and interactions of antipsychotics available in the BNF or manufacturer summaries of product characteristics (SPCs)

Relevant NICE Guidance


NICE CG 120. Psychosis with coexisting substance misuse (2011). http://www.nice.org.uk/guidance/cg120

### Pharmacological Treatments for Psychosis Schizophrenia (Acute exacerbation or recurrence of psychosis or schizophrenia)

<table>
<thead>
<tr>
<th>First Line:</th>
<th>Relative Cost</th>
<th>Notes</th>
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</thead>
</table>
| Any appropriate antipsychotic drug (see second and first generation antipsychotics and Appendix 1 below) | £-££££ | • NICE states that there is little evidence of any clinically significant differences in efficacy between antipsychotic drugs [except for clozapine in treatment-resistant schizophrenia]  
• For all acute episodes, prescribe oral antipsychotic in conjunction with psychological interventions OR review existing medication. The choice of antipsychotic should be determined by service user’s current symptoms, past medication history, response, comorbidities, concurrent treatments, side effects and importantly, individual preferences, taking into account carer views, where appropriate. |

<table>
<thead>
<tr>
<th>Second Generation Antipsychotics</th>
<th>Relative Cost</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Antipsychotics</td>
<td>Discuss benefits and side effects. Consider previous response; Ensure compliance and optimise dose.</td>
<td></td>
</tr>
</tbody>
</table>
| Risperidone  
Branded/Liquid | £ | Risk of dose-dependent EPSE; increases prolactin; hypotension, tachycardia, weight gain, hyperglycaemia can occur |
| Olanzapine  
Branded / Velotabs | £ | Weight gain and metabolic side effects are common; low EPS; smoking induces metabolism of olanzapine so stopping smoking can increase levels, possibly causing increased side effects |
| Quetiapine (MR / Branded ) | £ (£-£££) | Low risk of EPSE; M/R costly - to be reserved for defined clinical need e.g. compliance or side effects |
| Aripiprazole (Branded) | £ (£££) | Limited evidence of benefit above 15mg |
| Amisulpride (Liquid) | £ (££) | Marked prolactin elevation |
| Paliperidone palmitate  
Xeplion  
Trevicta (3-monthly) | £££££ | Consultant initiation only by written request to Chief Pharmacist; risk of EPSE and prolactin increase  
Not currently approved for general use. |
| Lurasidone | £££ | Consultant initiation only by written request to Chief Pharmacist. Alternative for metabolic side effects |
| Asenapine | £££ | Not currently approved for general use; Exceptional used by written request from consultants only |
| Paliperidone | £££ | Not currently approved for general use; Exceptional use by written request from a consultant only |

| Long-Acting Injections | | |
| Aripiprazole Abilify Maintena | £££££ | Consultant initiation only by written request to Chief Pharmacist; Administration, dosing and precautions as per BNF |
| Risperidone Risperdal Consta | ££££ | Complex pharmacokinetics – 3 week lag time to release of drug; antipsychotic cover or oral supplementation required; increases prolactin levels; increase risk of EPSE at higher doses |
| Paliperidone palmitate Xeplion  
Trevicta (3-monthly) | £££££ | Consultant initiation only by written request to Chief Pharmacist; risk of EPSE and prolactin increase  
Not currently approved for general use. |
| Olanzapine embonate Zypadhera | £££££ | Not currently recommended for general use due to post injection syndrome; Olanzapine can cause significant weight gain, hyperglycaemia, sedation and injection-related side effects |
# Pharmacological Treatments for Schizophrenia

<table>
<thead>
<tr>
<th>First Generation Antipsychotics</th>
<th>Relative Cost</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine liquid</td>
<td>£ ££</td>
<td>Highest incidence of sedation; potent anticholinergic effects, hypotension; can cause skin photosensitivity; Advise using sunscreen if necessary.</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>£</td>
<td>High risk of extrapyramidal side effects; also useful for agitation, aggression, impulsive behaviour</td>
</tr>
<tr>
<td>Flupentixol</td>
<td>££</td>
<td>Not recommended for excitable or agitated patients.</td>
</tr>
<tr>
<td>Sulpiride Liquid</td>
<td>£</td>
<td>Increased agitation reported at high dosage; care in mania/hypomania; Extrapyramidal side effects and hyperprolactinaemia common; beneficial in apathy and withdrawal</td>
</tr>
<tr>
<td>Promazine</td>
<td>££</td>
<td>Adjunctive treatment of psychomotor agitation and agitation/restlessness in the elderly</td>
</tr>
<tr>
<td>Benperidol</td>
<td>££</td>
<td>Licensed for control of deviant antisocial sexual behaviour only; Caution – ECG necessary</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>££</td>
<td>Alternative to chlorpromazine especially when it is desirable to reduce psychomotor activity.</td>
</tr>
<tr>
<td>Pericyazine (syrup)</td>
<td>££ (£££)</td>
<td>Also used as an adjunct in anxiety, agitation and violent or dangerously impulsive behaviour</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>££</td>
<td>Also used as an adjunct in anxiety, agitation and violent or dangerously impulsive behaviour</td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>££</td>
<td>High liability for extrapyramidal side effects</td>
</tr>
<tr>
<td>Zuclopenthixol (liquid)</td>
<td>£ (££)</td>
<td>Sedative drug; risk of extrapyramidal side effects</td>
</tr>
<tr>
<td><strong>Depot Injections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol decanoate</td>
<td>££</td>
<td>Longer-acting – suitable for monthly administration Higher incidence of EPSE; risk of QT prolongation and ventricular arrhythmias may be increased with high doses or parenteral use</td>
</tr>
<tr>
<td>Pipotiazine palmitate</td>
<td>££££</td>
<td>Phenothiazine antipsychotic; risk of antimuscarinic effects hypotension, cardiac arrhythmias, prolactin elevation, extrapyramidal effects, blood and hepatic disorders and photosensitivity</td>
</tr>
<tr>
<td>Flupentixol decanoate</td>
<td>£££</td>
<td>Not recommended for excitable or agitated people</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>££</td>
<td>Less likely to cause sedation, hypotension or antimuscarinic effects but high risk of EPSE</td>
</tr>
<tr>
<td>Zuclopenthixol decanoate</td>
<td>££</td>
<td>Do not give if depressed level of consciousness due to any cause</td>
</tr>
<tr>
<td><strong>Not Routinely Recommended</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pimozide</td>
<td>££</td>
<td>Not recommended due to risk of ECG changes, serious arrhythmia and sudden death</td>
</tr>
<tr>
<td>Fluspirilene depot</td>
<td>££</td>
<td>Unlicensed in the UK; Available to existing users on a named patient only basis; Consultant only</td>
</tr>
</tbody>
</table>
APPENDIX 1: Antipsychotic Selection Criteria

- There is little evidence of any clinically significant differences in efficacy between antipsychotic drugs except for superior efficacy of clozapine when used for schizophrenia that has not responded adequately to other antipsychotic medication.
- The choice of antipsychotic medication should be made by the service user and healthcare professional together, taking into account the views of the carer if the service user agrees.
- Consider the service user’s past medication history, clinical response, side effects, current symptoms, co-occurring conditions, concurrent treatments and individual preferences.
- Consider the side-effect profile of each drug, including extrapyramidal, metabolic, cardiovascular and hormonal and other side effects.
- Consider acquisition costs, particularly when more than one antipsychotic is suitable.
- Depot or long-acting injectable antipsychotics may be considered for people with psychosis or schizophrenia who would prefer such treatment after an acute episode of schizophrenia, or where avoiding covert non-adherence is a clinical priority.

NB: Aripiprazole, paliperidone and olanzapine® depot are reserved for consultant initiation only by written request to the Chief Pharmacist giving clear rationale for prescribing.

#Not currently approved by the D&T committee for general use. For exceptional requests, contact Pharmacy.

PRESCRIBE ORAL ANTIPSYCHOTICS
- For first episode of psychosis, acute exacerbation or recurrence of schizophrenia
- Where there are no concerns or problems with adherence/compliance
- For older adults
- For people with serious co-morbidities

PRESCRIBE DEPOT OR LONG-ACTING ANTIPSYCHOTICS
- Maintenance treatment with antipsychotic is needed
- When the service user prefers depot or long-acting antipsychotic treatment
- After previous good response to depot or long-acting antipsychotic treatment
- To avoid covert non-adherence where there is no compliance with oral treatment

CONSIDER A FIRST GENERATION ‘TYPICAL’ DEPOT ANTIPSYCHOTIC IF:
- Concerned about metabolic side effects
- No concerns about extrapyramidal effects
- No previous depot has been tried
- A flexible dose range and interval preferred
- Side effect profile and properties of depot make it appropriate
- There is history of previous good response
- Service user is experiencing intolerable side effects from an atypical long acting depot
- Service user prefers typical depot

CONSIDER A SECOND GENERATION ‘ATYPICAL’ LONG ACTING INJECTION IF:
- Concerned about extrapyramidal effects
- Good response and tolerability to the oral form of the injection formulation has previously been demonstrated
- Not concerned about metabolic side effects
- Service user has responded well to a typical depot preparation but is suffering from intolerable side effects
- Serious co-morbidities
- Clinical need for deltoid administration
- Informed service user preference
Managing Treatment Refractory Schizophrenia

<table>
<thead>
<tr>
<th>First Line:</th>
<th>Relative Cost</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Clozapine   | ££            | Review the diagnosis, check adherence and exclude other causes of non-response. Offer clozapine where there is inadequate response to treatment despite the sequential use of adequate doses of at least two different antipsychotic drugs including at least one second-generation antipsychotic prescribed for an adequate duration OR where there are unacceptable side effects from other medication. Registration with a clozapine monitoring service and routine blood monitoring are prerequisites for clozapine use because of the risk of neutropenia and agranulocytosis. Prescribers and Pharmacy must ensure that effective ongoing monitoring is maintained. Before starting clozapine:  
  - check adherence to antipsychotic medication  
  - ensure an adequate dose of antipsychotic has been prescribed and for an optimal duration  
  - check there has been an adequate trial of at least two antipsychotics or history of intolerance  
  - if not, consider switching to an alternative antipsychotic agent  
  - consider other causes of non-response, such as co-morbid substance misuse  
  - review engagement with and consider use of psychological treatments  
  - carry out baseline tests and register with monitoring service  
During treatment, monitor bloods and side effects, especially weight gain and metabolic effects. Prompt adjustment of clozapine dose is required when smoking stops. |

<table>
<thead>
<tr>
<th>Second Line:</th>
<th>Relative Cost</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>££-£££</td>
<td>Consider where there is a lack of or inadequate response clozapine at an optimized dose. Check adherence (including measuring plasma levels) and optimise the dose. Consider psychological treatments before adding a second antipsychotic. Choose an antipsychotic that does not worsen the common side effects of clozapine. Amisulpride and sulpiride are commonly tried. An adequate trial of such augmentation may need to be up to 8-10 weeks. Caution-combined antipsychotics may imply higher than necessary total dosage and an increased risk of side effects. Monitor and review benefits of clozapine augmentation regularly.</td>
</tr>
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</table>
### Managing Treatment Refractory Schizophrenia

#### Second Line:

<table>
<thead>
<tr>
<th>Relative Cost</th>
<th>Notes</th>
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<tbody>
<tr>
<td>££-£££</td>
<td>-</td>
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<tr>
<td>££-££££</td>
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</table>

- Choose a drug that does not compound the common side effects of clozapine.
- Aripiprazole has been tried for positive symptoms and metabolic side effects. Limited evidence.
- Use lower doses; regularly monitor side effects and physical health. Discontinue if not beneficial.

- Limited evidence; Augmentation with mood stabilisers (valproate and lamotrigine), antidepressants (SSRIs, mirtazapine) and benzodiazepines may be tried, if clinically indicated.

#### Other strategies

<table>
<thead>
<tr>
<th>Relative Cost</th>
<th>Notes</th>
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<tbody>
<tr>
<td>££-££££</td>
<td>-</td>
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</table>

- There is little supportive evidence for superior efficacy but increased risk of side effects
- Combination use should be reserved to short periods during switching antipsychotics.
- Only use combinations of antipsychotics where there are no obvious problems with use and as for an adequate therapeutic trial.
- Document reasons for use fully and monitor treatment outcome regularly
- Aripiprazole may reduce prolactin when used in combination with antipsychotics that raise prolactin
- Review continued use of combinations regularly and discontinue if no clinical benefits are apparent.

- Limited evidence of benefit. Use for a specified therapeutic trial and discontinue if not beneficial.
- Carbamazepine has been used to improve behaviour or aggression but risk of drug interactions
- Benzodiazepine can reduce anxiety but risk of dependence; Short-term use only
- SSRIs or mirtazapine can improve negative or depressive symptoms
- There is limited data for valproate and lithium augmentation but they may be tried for specific cases

- There is little good evidence to support the use of high dosage of a single antipsychotic or combinations of antipsychotics. Routine use of high-dose antipsychotics is not recommended.
- There is an increased risk of side effects
- Justification for high dose treatment should be documented in the case notes.
- If used, this should only be after evidence-based strategies have failed, and as a carefully monitored therapeutic trial
- Follow advice in Royal College of Psychiatrists [Consensus guideline on High Dose Antipsychotics](#).
# Appendix 1

## Long-Acting and Depot Antipsychotic Injections

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Dose and Administration</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **Aripiprazole powder and solvent for prolonged-release suspension for injection Abilify Maintena 400 mg** | - Recommended starting and maintenance dose is 400mg. If adverse reactions occur with 400mg, a dose of 300mg once monthly should be considered.  
- Dosing interval monthly (no sooner than 26 days after the previous injection).  
- Route of administration intramuscular injection into the gluteal muscle  
- Dose adjustments may be required due to drug interactions  
- Tolerability to oral aripiprazole should be established prior to the injection  
- Oral aripiprazole at 10mg-20mg per day must continue for two weeks after the first injection | - Consultant initiation only, by written request to the chief pharmacist.  
- Maintenance in schizophrenia in patients stabilised with oral aripiprazole  
- Safety and efficacy of aripiprazole PR injection in children and adolescents up to 17 years and adults ≥65 years have not been established. Therefore its use in these group is not recommended  
- Requires reconstitution prior administration  
- Gluteal or deltoid muscle  
- Stored at room temperature  
- Requires 2 weeks oral supplementation with aripiprazole  
- Lower risk of weight gain, hyperprolactinaemia, EPSE and metabolic adverse effects  
- Higher frequency of extrapyramidal side effects with aripiprazole prolonged release injection 400/300 mg injection compared to oral aripiprazole 10-30mg in clinical trials |
| **Flupentixol decanoate In thin vegetable oil (derived from coconuts) Depixol®; Psytiol® Available strengths 20mg in 1ml; 100mg in 1ml; 200mg in 1ml** | - Dosing interval 1-4 weeks  
- Test dose 20mg;  
- Usual dose 50mg every 4 weeks to 300mg every 2 weeks; Max 400mg/week  
- Elderly/debilitated - ¼ to ½ adult dose  
- Administer by deep intramuscular (IM) injection only into the upper outer buttock (dorsogluteal) or lateral thigh (vastus lateralis)  
- Maximum volume per site should not exceed 2ml | - Maintenance in schizophrenia in patients stabilised with oral antipsychotics  
- Flexible dosing regime/intervals  
- Requires small test dose of the injection  
- Does not require reconstitution prior administration  
- Oil based injection  
- Gluteal or lateral thigh administration  
- Mood elevating |
### Long-Acting and Depot Antipsychotic Injections

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Dose and Administration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluphenazine decanoate</strong>&lt;br&gt;In sesame oil&lt;br&gt;Modecate®&lt;br&gt;Available strengths 25mg in 1ml; 100mg in 1ml</td>
<td>- Dosing interval 2-5 weeks&lt;br&gt;- Test dose 12.5mg (elderly 6.25mg)&lt;br&gt;- Usual dose 12.5mg (6.25mg for over 60s) to 100mg every 2-5 weeks&lt;br&gt;- Administer by deep intramuscular injection into the gluteal muscle</td>
<td>- Maintenance in schizophrenia in patient stabilized on oral antipsychotics&lt;br&gt;- Flexible dosing regime/intervals&lt;br&gt;- Requires small test dose of the injection&lt;br&gt;- Does not require reconstitution prior administration&lt;br&gt;- Oil based injection&lt;br&gt;- Gluteal administration only&lt;br&gt;- Onset of action between 24 and 72 hours after injection&lt;br&gt;- Effects on psychotic symptoms significant within 48 to 96 hours&lt;br&gt;- High frequency of extrapyramidal effects</td>
</tr>
<tr>
<td><strong>Fluspirilene</strong>&lt;br&gt;In water for Injection&lt;br&gt;Imap®; Redeptin®&lt;br&gt;Available strengths 2mg in 1ml</td>
<td>- Dosing interval - weekly&lt;br&gt;- 2-10mg once a week&lt;br&gt;- Maintenance dose is usually 4-8mg;&lt;br&gt;- Higher doses may be required&lt;br&gt;- Elderly – use lower doses&lt;br&gt;- Administer by deep intramuscular injection into the gluteal muscle&lt;br&gt;- Max volume per site should not exceed 2ml</td>
<td>- Unlicensed – named patient only.&lt;br&gt;- In use mainly for continuation in existing patients.&lt;br&gt;- Maintenance in schizophrenia in patient stabilized with oral antipsychotics&lt;br&gt;- Water-based injection&lt;br&gt;- Weekly administration</td>
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<td><strong>Haloperidol decanoate</strong>&lt;br&gt;In sesame oil&lt;br&gt;Haldol®&lt;br&gt;Available strengths 50mg in 1ml; 100mg in 1ml</td>
<td>- Dosing interval - 4 weekly (*halve doses if 2-weekly administration)&lt;br&gt;- Test dose 25mg (12.5mg in the elderly)&lt;br&gt;- Usual dose range 50mg every 4 weeks to 300mg every 4 weeks&lt;br&gt;- Administer by deep intramuscular injection into the gluteal muscle using an appropriate needle, preferably 2-2.5 inches long, at least 21 gauge&lt;br&gt;- Max volume per site – 3ml</td>
<td>- Maintenance in schizophrenia in patient stabilized with oral antipsychotics&lt;br&gt;- Monthly interval of administration.&lt;br&gt;- Does not require reconstitution prior administration&lt;br&gt;- Oil based injection&lt;br&gt;- Gluteal administration only&lt;br&gt;- High risk in cardiovascular disease&lt;br&gt;- High risk of EPSE</td>
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### Appendix 1 (continued)

#### Long-Acting (Depot) Antipsychotic Injections

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<th>Antipsychotic</th>
<th>Dose</th>
<th>Notes</th>
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<tr>
<td>Olanzapine pamoate monohydrate powder for suspension Zypadhera®</td>
<td>Dosing interval – 2-4 weekly&lt;br&gt; Dose 210mg – 300mg every 2 weeks; Dose may be adjusted to allow 4 weekly administration.&lt;br&gt; No test dose; Pre-treat with oral olanzapine in order to establish tolerability and response&lt;br&gt; Route: Deep intramuscular gluteal injection</td>
<td>Not currently approved for use due to post-injection syndrome&lt;br&gt; After each injection, service users should be observed in a healthcare facility by appropriately qualified personnel for at least 3 hours for signs and symptoms consistent with olanzapine overdose.&lt;br&gt; Not recommended in &gt;75 years&lt;br&gt; Low risk or EPSE&lt;br&gt; High risk of weight gain</td>
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<td>Paliperidone palmitate Xeplion®</td>
<td>Dosing interval - monthly&lt;br&gt; No test dose; Establish tolerability with oral paliperidone or risperidone prior to initiating paliperidone palmitate&lt;br&gt; Initiation regime - Day 1-150mg IM; Day 8: 100mg IM via deltoid.&lt;br&gt; Maintenance dose is 75 mg; range of 25 to 150 mg deltoid or gluteal.&lt;br&gt; Initiation regime not required for people switching from depot or long-acting injections&lt;br&gt; the SPC provides the information on equivalent dose to risperidone long acting injection&lt;br&gt; Administration is by deep intramuscular injection via deltoid or gluteal muscle using safety needles provided&lt;br&gt; The dose should not be given in divided injections&lt;br&gt; Fractions of dose not possible.</td>
<td>Consultant initiation only, by written request to the chief pharmacist.&lt;br&gt; Maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone.&lt;br&gt; Not recommended in people with moderate or severe renal impairment, or older adults (&gt;65yo)&lt;br&gt; No reconstitution needed&lt;br&gt; No initial oral supplementation required&lt;br&gt; Monthly injections&lt;br&gt; Choice of gluteal or deltoid administration&lt;br&gt; Less EPSE at lower doses&lt;br&gt; Release of the active substance starts as early as day 1, peaks at day 14 and lasts for at least 4 months</td>
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## Long- Acting (Depot) Antipsychotic Injections

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</table>
| Pipotiazine palmitate In sesame oil Piportil® | • Dosing interval - 4 weekly  
• Test dose 25mg (elderly 5–10mg)  
50mg (5–10mg in elderly) to 100mg every 4 weeks  
• Max. 200mg every 4 weeks (NB: large volume and 2 injections may be required)  
• Administer by deep intramuscular injection into the gluteal muscle | • Discontinued in March 2015.  
• No new patient should be initiated on pipotiazine  
• Maintenance in schizophrenia in patient stabilized with oral antipsychotics  
• Monthly interval administration.  
• Does not require reconstitution prior administration  
• Oil based injection  
• Gluteal injection only  
• Low incidence of EPSE |
| Risperidone powder and solvent for prolonged-release suspension Risperdal Consta® | • Dosing interval - 2 weekly  
• No test dose but pretreat with oral for 1-2 days to confirm tolerability if no previous use of risperidone  
• Usual dose range 25mg -50mg every two weeks  
• Max. Dose:50mg every 2 weeks  
• Administer by deep intramuscular gluteal or deltoid injection using the provided safety needle  
• Fractions of a dose not possible  
• Dose increases after at least 4 weeks | • Maintenance treatment of schizophrenia in adult patients stabilised with antipsychotics.  
• Prior test tolerance with oral tablets  
• Refrigerated storage required  
• Needs reconstituting  
• Complex pharmacokinetics - lag time of 3 weeks before drug release. Oral antipsychotic cover required during the first 3 weeks of treatment  
• No flexibility in dosing or interval  
• Gluteal or deltoid injection  
• Less EPSE at lower doses  
• Choice of gluteal or deltoid administration |
| Zuclopenthixol decanoate In thin vegetable oil (derived from coconuts) Clopixol | • Dosing interval – 1-4 weekly  
• Test dose 100mg (elderly 25-50mg)  
• Usual dose 200mg -500mg every 1 to 4 weeks  
• Elderly/debilitated - ¼ to ½ adult dose  
• Max: 600mg every week  
• Administer by deep intramuscular injection into the upper outer buttock (dorsogluteal) or lateral thigh (vastus lateralis)  
• Max volume per site should not exceed 2ml | • Maintenance treatment of schizophrenia in adult patients stabilised with antipsychotics.  
• Flexible dosing regime/intervals  
• Requires small test dose of the injection  
• Does not require reconstitution prior administration  
• Oil based injection  
• Gluteal or thigh administration  
• May be more effective in preventing relapses than other conventional antipsychotic depot preparations |
### Relative Antipsychotic Side Effects

<table>
<thead>
<tr>
<th>FGA Drug</th>
<th>Side Effect</th>
<th>Anticholinergic</th>
<th>Cardiac QT effect</th>
<th>Hypotension</th>
<th>Sedation</th>
<th>Weight</th>
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<th>Prolactin</th>
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**Key:**
- Anticholinergic effects includes symptoms commonly caused by muscarinic receptor blockade e.g. dry mouth, sweating, blurred vision, constipation and urinary retention
- +++ = relatively common;
- ++ = moderately common
- + = uncommon
- +/- = little or no effect
- blank = unknown or insufficient information
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Rankings compiled using information available from various sources

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References


7. The Maudsley Guidelines 12th edition. Also available online at: http://www.library.nhs.uk/booksandjournals/ebooks/ (Open Athens password required)

8. BNF 72. Available online at: https://www.medicinescomplete.com/mc/bnf/current/


10. Manufacturer Summaries of Product Characteristics (SPCs) for the medicines listed in this document can be found in the Electronic Medicines Compendium (http://www.medicines.org.uk/emc/).