Prescribing guidelines for the use of antipsychotic drugs in the treatment of schizophrenia and psychosis.

Initiation of treatment is likely to be carried out by a specialist, however these guidelines are also intended to provide information to support GPs in the continued prescribing of these drugs.

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Treatment of psychosis and schizophrenia algorithm

Notes:

1. See appendix 3 for information on relative drug effects which may influence choice.

2. Decide which antipsychotic to use in partnership with the service user &/or carer based on relative risk of adverse effects

3. Max Risperidone dose in BNF is 16mg daily, yet doses above 8mg daily are rarely used in secondary care. Higher doses are more likely to cause EPSE and other side effects.

4. Quetiapine XL is used in secondary care to initiate treatment. Patients can switch immediately to IR upon discharge without adverse effect.

Psychotic symptoms may be due to an autoimmune process. Please follow the recommendations for antibody screening on page 2

First choice: See prescribing advice on following pages, BNF for dose guidance, and Notes (on left)
Oral risperidone (as per Lavender statement) or, if risperidone is not suitable: amisulpride, olanzapine, quetiapine, or any typical antipsychotic (in alphabetical order).
If all else is equal choose the antipsychotic with the lowest acquisition cost (see appendix 1)

Introduce drug gradually. Trial of at least 4 to 6 weeks at a therapeutic dose is recommended

Second choice: (due to NON RESPONSE)
Choose a different antipsychotic to that which has already been tried from (listed alphabetically): oral amisulpride, olanzapine, quetiapine, risperidone, or any typical antipsychotic. (Note: if a typical antipsychotic has already been tried then an atypical should be tried next)[1]

Second choice (due to POOR TOLERABILITY):
Choose a different antipsychotic to that which has caused poor tolerability based on the table below from the following (listed alphabetically): oral amisulpride, aripiprazole, olanzapine, quetiapine, risperidone, or typical.

Guidance on switching antipsychotics because of poor tolerability (listed alphabetically):

	Best choice	Other choices
Weight gain / Metabolic side effects	amisulpride, aripiprazole, haloperidol, trifluoperazine,	quetiapine, risperidone
Hyperprolactinaemia*	aripiprazole, quetiapine	clozapine (third line only), olanzapine
Akathisia	quetiapine	Clozapine (third line only)
Dystonias and other EPSEs	aripiprazole, olanzapine quetiapine	clozapine (third line only), risperidone (<4mg/day)
Drowsiness	amisulpride, aripiprazole, sulpiride	haloperidol, risperidone, trifluoperazine

*please refer to Trust hyperprolactinaemia guidelines.

Third choice: (due to POOR TOLERABILITY)
Oral aripiprazole, amisulpride, clozapine olanzapine, quetiapine, risperidone, or typical antipsychotic (listed alphabetically)

Third choice:
(due to NON RESPONSE)
Offer clozapine.

Depot & long-acting injection (LAI) antipsychotics:

Depot and LAI antipsychotics are offered to patients who cannot or will not agree to take oral medication regularly.
Typical depot antipsychotics are offered as FIRST CHOICE.
Atypical depot antipsychotics are restricted within the Trust to the following patient groups:

1. Those who are unable to comply with oral treatment, but have shown a good response to oral atypical antipsychotics AND have never been treated with typical antipsychotics
2. Those who have responded well to an oral or depot typical antipsychotic but suffer an unacceptably high level of side effects related to this class of antipsychotic.

Atypical antipsychotic depots used in the Trust (secondary care prescribing only):
Paliperidone palmitate (Xeplion®) – Note: oral paliperidone (Invega®) is not used.
Aripiprazole (Abilify Maintena®)
Risperidone LAI (Risperdal Consta®)
Olanzapine pamoate (Zypadhera®) – Note: must be administered in a healthcare setting

Special Populations:

Choice of treatment may vary for specific populations. For further advice on prescribing in patients <18 or >65, or in pregnancy, lactation, epilepsy, hepatic or renal impairment, cardiovascular or Parkinson's disease or diabetes, contact Medicines Information:
Med.Info@oxfordhealth.nhs.uk
Tel: 01865 455716

For prescribing in CAMHS see also: NICE BITES Mar 2013 No.50. Psychosis and Schizophrenia in children and young adults:
www.medicinesresources.nhs.uk

Antipsychotic drugs are used for a variety of different indications however these guidelines address the treatment of schizophrenia and psychosis only.
All antipsychotics are effective treatments in the acute and maintenance phase of the illness however as they all differ in their pharmacology and side effect profiles choice is determined on an individual case by case basis. The National Institute for Clinical Excellence (NICE) emphasises the need to involve the patient in the decisions made about treatment choice and this should be done wherever possible.

Summary of NICE guidance[1]:

- For people with newly diagnosed schizophrenia, offer oral antipsychotic medication. Provide information and discuss the benefits and side-effect profile of each drug with the service user. The choice of drug should be made by the service user and healthcare professional together, considering:
  - the relative potential of individual antipsychotic drugs to cause extrapyramidal side effects (including akathisia), metabolic side effects (including weight gain) and other side effects (including unpleasant subjective experiences)
  - the views of the carer if the service user agrees.

- Before starting antipsychotic medication, offer the person with schizophrenia an electrocardiogram (ECG) if:
  - specified in the SPC
  - a physical examination has identified specific cardiovascular risk (such as diagnosis of high blood pressure)
  - there is personal history of cardiovascular disease, or
  - the service user is being admitted as an inpatient.

- Consider treatment with antipsychotic medication as an individual therapeutic trial:
  - Record the indications, expected benefits and risks, and expected time for a change in symptoms and for side effects to occur.
  - Start with a dose at the lower end of the licensed range and titrate upwards slowly within the dose range specified in the British National Formulary (BNF) or SPC.
  - Justify and record reasons for dosages outside the range specified in the BNF or SPC (*and follow guidelines for High Dose Antipsychotic Treatment Monitoring where appropriate – see Oxford Health NHSFT HDAT monitoring guideline*)
  - Monitor and record the following regularly and systematically throughout treatment, but especially during titration:
    - efficacy, including changes in symptoms and behaviour
    - side effects of treatment, taking into account overlap with some of the clinical features of schizophrenia
    - adherence
    - physical health
- Record the rationale for continuing, changing or stopping medication and the effects of such changes
- Carry out a trial of the medication at optimum dosage for 4-6 weeks

- Consider offering depot/long-acting injectable antipsychotics when:
  - Service users would prefer such treatment after an acute episode
  - avoiding covert non-adherence to medication is a clinical priority

- Inform service users about the high risk of relapse if medication is stopped in 1-2 years. If withdrawing antipsychotic medication, do this gradually. Regularly monitor for signs and symptoms of relapse for at least 2 years after withdrawal.

Do	Don't
Discuss with the service user, and carer if appropriate: ○ Any non-prescribed therapies (including complementary therapies) the service user wishes to use ○ Alcohol, tobacco, prescription and non-prescription medication and illicit drugs Discuss their possible interference with the effects of prescribed medication and psychological treatments. Discuss the safety and efficacy of non-prescribed therapies	Do not use a loading dose of antipsychotic medication ('rapid neuroleptisation'). NB this does not apply to loading doses of paliperidone and olanzapine depots, which are described in the product literature for drug initiation.
Warn of a potential photosensitive skin response with chlorpromazine and advise using sunscreen if necessary	Do not initiate regular combined antipsychotic medication, except for short periods (for example, when changing medication).

Inadequate response
Offer clozapine to people with schizophrenia whose illness has not responded adequately to treatment despite the sequential use of adequate doses of at least two different antipsychotic drugs. At least one of the drugs should be a non-clozapine second generation antipsychotic. [See following page for information on clozapine shared care]
If symptoms have not responded adequately to an optimised dose of clozapine, review the diagnosis, adherence to treatment, engagement with and use of psychological treatments, other possible causes of non-response and measure therapeutic drug levels before offering a second antipsychotic to augment clozapine. The second drug should not compound the common side effects of clozapine. An adequate trial of augmentation may need to be up to 8-10 weeks.

Screening for antibodies
Psychotic symptoms may be due to an autoimmune process. Screening for anti-NMDAR and anti-VGKC autoantibodies is indicated in all patients if w*ithin 3 months of an acute psychotic presentation, if not previously tested.*

It is recommended that samples are sent to Immunology at the John Radcliffe Hospital in a red-top serum blood tube with clinical details and request for NMDAR and VGKC autoantibodies.

Treatment for psychosis should be with antipsychotics while screening results are awaited. Positive results and queries can be discussed with Dr Belinda Lennox (Belinda.lennox@oxfordhealth.nhs.uk) regarding ongoing management. Treatment with antipsychotics as per the treatment guideline should continue until advice is given by Dr Lennox. This recommendation applies to all age groups. Screening is provided free of charge and any changes in cost implications will require a review of screening for antibodies.

Prescribing advice

Carry out all necessary baseline physical monitoring prior to commencing an antipsychotic – refer to recommendations in the Oxford Health NHS FT Psychotropic Monitoring Guidelines[2] for individual drugs and to appendix 2 ("General Psychotropic Medication Monitoring") [see also below for excerpt]. GPs should refer to Good Practice Monitoring Guidelines for Severe Mental Illness on the Oxford CCG website)

- If all else is equal choose the antipsychotic with the lowest acquisition cost (see appendix 1 for comparisons)
- The lowest possible dose should be used. Titrate the dose to the lowest known dose to be effective (see appendix 2). After two weeks increase the dose only if the patient shows poor or no response. [NB depot antipsychotics – plasma levels rise for 6-12 weeks after initiation, even without dose changes]
- For choice of antipsychotic follow treatment algorithm on the first page.
- The use of a single antipsychotic drug is recommended for the majority of patients. Antipsychotic polypharmacy should be avoided due to increased cardiac risk.
- Responses to antipsychotic drug treatment should be assessed using validated rating scales e.g. Clinical Global Impression Scale (CGI)
- Close monitoring of physical health should be undertaken (refer to Oxford Health NHS FT Psychotropic Monitoring Guidelines (see also excerpt below) and for GPs see Good Practice Monitoring Guidelines for Severe Mental Illness on the Oxford CCG website)

Physical Health Monitoring[2]

Baseline Observations:

- BP and pulse
- FBC
- Urea & electrolytes, including serum creatinine (and request eGFR)
- LFTs
- Basic urine screen
- TSH
- Weight
- Height (calculate BMI)
- Waist circumference (if BMI between 25-35.5kg/m^2)
- Fasting lipid profile including triglycerides
- Fasting glucose (random if not possible)
- HbA1c – ONLY if fasting glucose levels raised on 2 occasions (refer to NICE diabetes guideline where indicated)
- Pregnancy test
- Urine drug screen
- Enquire about alcohol intake
- ECG (where indicated by individual risk factors)

Yearly monitoring

- BMI
- Waist circumference (if BMI between 25-35.5 Kg/m^2)
- BP and pulse
- Fasting lipids (random if not possible) including triglycerides (TG), HDL-C and Cholesterol ratio
- Fasting glucose (random if not possible)
- Smoking and alcohol intake

Further monitoring

- Repeat as clinical need dictates or as specified in the individual drug monograph in the tables on the following pages
- Mental state should be closely monitored during treatment - consideration should be given to the possibility that some medicines may adversely affect mental state e.g. antidepressants causing manic or hypomanic episodes, the appearance or worsening of suicide-related behaviours with drugs such as atomoxetine and the SSRIs.

Patient information

Up to date information for patients and carers can be accessed at www.choiceandmedication.org.uk/oxfordhealth

Shared care

Shared care arrangements for the prescribing of antipsychotic drugs should be encouraged as it promotes the principles of recovery and social inclusion, as well as reducing risk and improving physical health.
Shared care guidelines for clozapine are in place in Oxfordshire and are available on the CCG website.

References:

1. Core interventions in the treatment and management of schizophrenia in adults in primary and secondary care, CG82, NICE 2009
2. Oxford Health NHS FT Psychotropic Monitoring Guidelines, 2010
3. Regional Drugs & therapeutics Centre. Cost comparison charts April 2013. Accessed online at: http://www.nyrdtc.nhs.uk
4. NHS Electronic Drug Tariff. Accessed 26th September 2013 online at: http://www.ppa.org.uk
5. Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry, 11th edition, Wiley Blackwell 2012
6. Bazire S. Psychotropic Drug Directory. Lloyd-Reinhold Communications 2012

Appendix 1 – Atypical antipsychotics – maintenance doses (adults with psychosis) – cost of 1 year's treatment (using Drug Tariff prices). Doses are not intended to imply therapeutic equivalence.[3,4]

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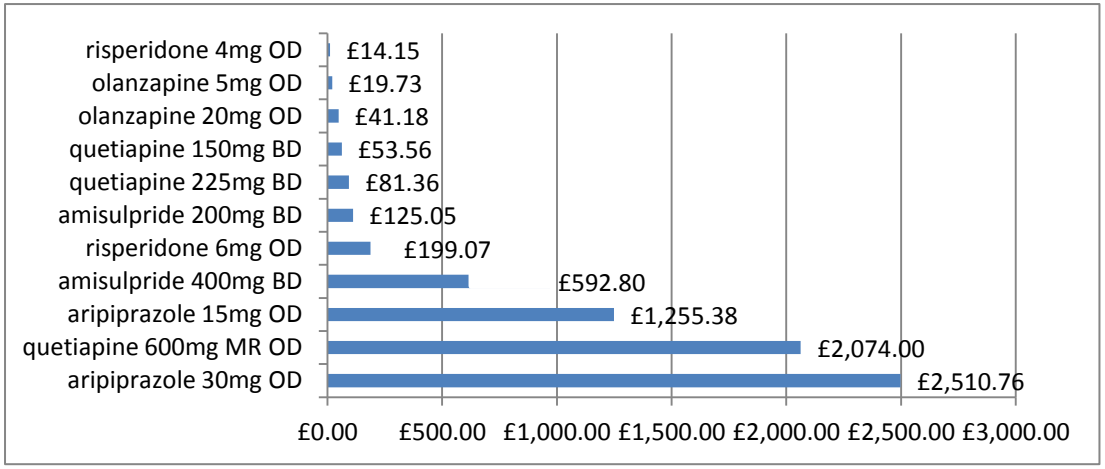

Appendix 2 - Minimum effective daily dose of antipsychotics[4]

Antipsychotic	First episode dose (mg)	Relapse /exacerbation dose (mg)
Chlorpromazine	200	300
Haloperidol	2	>4
Sulpiride	400	800
Trifluoperazine	10	15
Amisulpride	400	800
Aripiprazole	10	10
Asenapine	10	10
Olanzapine	5	10
Quetiapine	150	300
Risperidone	2	3

Appendix 3 - Relative risk of adverse effects[5,6]

Antipsychotic	Sedation	Extrapyramidal effects	Anticholinergic effects	Risk of developing diabetes	Weight gain	Hypotension	Cardiac	hyperprolactinaemia
Amisulpiride	♦	♦♦	♦	♦♦	♦♦	♦	♦	♦♦♦♦
Aripiprazole	♦	♦	♦	♦	♦	♦	♦♦	♦
Asenapine	♦♦	♦	♦	♦	♦♦	♦		♦♦
Chlorpromazine	♦♦♦♦	♦♦♦	♦♦♦	♦♦♦	♦♦♦	♦♦♦♦	♦♦♦	♦♦♦♦
Clozapine	♦♦♦♦	♦	♦♦♦♦	♦♦♦♦	♦♦♦♦	♦♦♦♦	♦♦♦♦	♦
Flupentixol	♦♦	♦♦♦	♦♦♦	♦♦	♦♦♦	♦♦	♦	♦♦♦♦
Fluphenazine	♦♦	♦♦♦♦	♦♦♦	♦♦	♦♦	♦♦	♦	♦♦♦♦
Haloperidol	♦♦	♦♦♦♦	♦♦	♦	♦♦	♦♦	♦♦♦	♦♦♦♦
Olanzapine	♦♦♦	♦	♦♦	♦♦♦♦	♦♦♦♦	♦♦	♦	♦♦
Paliperidone	♦♦	♦♦	♦♦	♦♦	♦♦♦	♦♦♦	♦	♦♦♦♦
Perphenazine	♦♦	♦♦♦♦	♦♦	♦	♦♦	♦♦	♦♦	♦♦♦♦
Pericyazine	♦♦♦♦	♦	♦			♦♦♦	♦♦♦	♦♦♦♦
Pimozide	♦♦	♦♦	♦♦	♦	♦♦	♦♦	♦♦♦♦	♦♦♦♦
Pipothiazine	♦♦♦	♦♦♦	♦♦♦	♦♦	♦♦♦	♦♦♦		♦♦♦♦
Promazine	♦♦♦♦	♦♦	♦♦♦	♦♦	♦♦♦	♦♦♦	♦♦♦	♦♦♦
Quetiapine	♦♦♦	♦	♦♦	♦♦♦	♦♦♦	♦♦♦	♦♦	♦
Risperidone	♦♦	♦♦	♦♦	♦♦	♦♦♦	♦♦♦	♦	♦♦♦♦
Sulpiride	♦	♦♦	♦	♦♦	♦♦	♦	♦	♦♦♦♦
Trifluoperazine	♦♦	♦♦♦♦	♦	♦	♦♦	♦♦	♦♦♦	♦♦♦♦
Zuclopenthixol	♦♦♦	♦♦♦	♦♦♦	♦♦	♦♦♦	♦♦	♦♦	♦♦♦♦

♦ - little/nothing; ♦♦ = mild; ♦♦♦ = moderate; ♦♦♦♦ = severe/marked

Guideline written by Rachel Brown, Clinical Lead Pharmacist and Orla MacDonald, Clinical Trials Pharmacist
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