Antipsychotics

Traffic light classification - Amber 2
Prescribing Guideline for Primary Care Prescribers

Scope

This prescribing guideline is for the use of antipsychotic medication (excluding clozapine) in the context of mental illness.

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Therapeutic Summary

NICE guidance for psychosis and schizophrenia in adults does not specifically recommend an antipsychotic class or individual antipsychotic as first-line treatment for schizophrenia but instead emphasises the importance of patient choice (taking into account adverse effects and service user/carer views where possible)[1].

NICE guidance for Bipolar Disorder recommends Haloperidol, Olanzapine, Risperidone or Quetiapine for the treatment of mania or hypomania (taking into account patient preference, any advance statements and clinical context)[2]. For moderate to severe bipolar depression, Olanzapine (either on its own or combined with Fluoxetine) or Quetiapine are the antipsychotics recommended by NICE. NICE guidance for bipolar disorder does not make any specific reference to the use of Aripiprazole in adult bipolar disorder but does refer to the NICE technology appraisal guidance (TAG)[3] on Aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder.

NICE guidance for depression in adults suggests an antipsychotic such as Aripiprazole, Olanzapine, Quetiapine or Risperidone as augmentation to antidepressant therapy[4]. Modified-release Quetiapine is licensed as an adjunct in the treatment of major depression; this is an off-label use of other antipsychotics. Note that oral Flupentixol is also licensed for use in depressive illness but rarely used.

NICE guidance for obsessive-compulsive disorder suggests an antipsychotic (in addition to a SSRI or Clomipramine) as a treatment option when other strategies have failed[5].

Antipsychotics may be prescribed for patients with dementia who are experiencing agitation, hallucinations or delusions that are causing them severe distress[6]. Refer to the Nottinghamshire APC Dementia - managing behavioural and psychological symptoms guideline.

Long-acting intramuscular (depot) antipsychotic injections are licensed for the maintenance treatment of schizophrenia and other psychoses. Depot antipsychotic injections are a useful option when compliance with oral antipsychotic treatment is unreliable[1].

Antipsychotic Initiation

Oral antipsychotics should not be started in primary care unless in consultation with a specialist.

Depot antipsychotics should only be initiated by specialist secondary care mental health services. A small test dose is given initially and the patient observed for side-effects. If there have not been any problems 4-7 days following the test dose the dose can be gradually titrated to the lowest effective maintenance dose. In the case of Aripiprazole, Paliperidone and Risperidone there are no injectable test doses so patients are given a small dose of the oral antipsychotic to assess tolerability.

Prescribing of antipsychotics for off-label indications should not be transferred to primary care unless upheld within a nationally recognised formulary such as the BNF, BNFC or national guidance such as NICE guidelines. This should be discussed and agreed with the GP prior to the transfer of prescribing.

Appendix one outlines the criteria for transferring antipsychotic prescribing to primary care.

Administration of Depot Injections

Practitioners must have the necessary knowledge, skills and competency to safely administer depot antipsychotic injections by deep intramuscular injection using the "z-track technique". Take particular care when selecting the needle gauge and length to ensure the drug is given deep into the muscle. For obese patients a longer 2-inch 20g/21g needle should be selected for gluteal administration and a 1.5-inch 22g needle for deltoid administration.

Reduction of local injection site reactions

- Use the lowest practical volume
- Inject less frequently if possible to prevent hard plaques of tissue forming.
- Use the Z-tracking technique to avoid extravasation
- Use a needle of the right length for the patient to ensure deep intramuscular administration (longer needles are required for people with a higher body mass index (BMI))
- Use alternate buttocks or arms (rotate injection sites) to allow time to heal. Note that not all depot antipsychotic injections are licensed for administration into the deltoid muscle.

Duration of Treatment

As stated in NICE guidance, following the treatment of an acute episode of psychosis, the risk of relapse is high if antipsychotic medication is stopped within 1 to 2 years[1]. For bipolar disorder treatment should be reviewed within 4 weeks of resolution of symptoms and if continued, reviewed every 3-6 months[2].

Monitoring Requirements and Responsibilities

During antipsychotic treatment, improvement in the patient's clinical condition may take several days to some weeks. Throughout this period the patient should be closely monitored. Please note that the occurrence of suicidal behaviour is inherent in psychotic illnesses and mood disorders, and in some cases has been reported early after initiation or switch of antipsychotic therapy. High risk patients should be closely supervised during treatment.

Secondary care should maintain responsibility for monitoring physical health and the effects of antipsychotic medication for at least the first 12 months or until the person's condition has stabilised. However, GP input may be sought if concerns are identified with the patient's physical health during this time. Thereafter, the responsibility for this monitoring may be transferred to primary care.

GPs and other primary healthcare professionals should monitor the physical health of people prescribed antipsychotic medication when responsibility for monitoring is transferred from secondary care, and then at least annually[1,2]. See Appendix two for the recommended general monitoring requirements and physical health monitoring schedule.

ECG Monitoring

A baseline ECG should be considered for all patients but is recommended by NICE[1,2] in the following scenarios:

- Specified in the SPC of the prescribed medication
- Physical examination has identified cardiovascular risk
- There is a personal history of cardiovascular disease
- The service user is admitted as an inpatient

Antipsychotics may prolong the QTc interval. Particular caution is required in the following instances[7]:

- Antipsychotic co-prescribed with other medicines that can prolong the QTc interval
- Antipsychotic prescribed above the BNF dose limit (high dose antipsychotic therapy)
- Underlying cardiac disease (e.g. ischaemic heart disease, congestive heart failure, bradycardia, personal history of long QTc, left ventricular hypertrophy)
- Family history of long QTc
- Severe renal or severe hepatic impairment
- Physiological risk factors for long QTc and arrhythmia (hypokalaemia, hypomagnesaemia, hypocalcaemia, anorexia nervosa, extreme of age, stress, shock, female gender and extreme physical exertion).
- Co-existing alcohol or substance misuse

Annual ECG monitoring should take place if any of these risk factors are present or if there has been a previous abnormality. More regular ECG monitoring may be indicated.

Management of QTc prolongation in patients prescribed antipsychotics[7,8]	
QTc	Action
<440ms (men) or <460ms (women)*	• No action required unless other ECG abnormalities
>440ms (men) or >460ms (women) but <500ms**	• Repeat ECG (consider checking the QTc calculation manually in case of machine error) • Check for other prescribed medication which can lengthen the QTc interval – www.crediblemeds.org • Check electrolytes – potassium, magnesium and calcium • Discuss with the specialist mental health team – may consider dose reduction or switching to an antipsychotic with less effect on QTc • Discuss with cardiology if in doubt
>500ms	• Red flag - immediate action required • Repeat ECG (consider checking the QTc calculation manually in case of machine error) • Check for other prescribed medication which can lengthen the QTc interval – www.crediblemeds.org • Stop the suspected causative drug(s) • Check electrolytes – potassium, magnesium and calcium • Discuss with the specialist mental health team • Discuss with cardiology

*Widely recognised QTc limits can't be applied in patients with atrial fibrillation, bundle branch block, paced rhythm, excessive tachycardia or bradycardia.

**There is no validity in an ECG acquired in the context of resting right or left bundle branch block as the QT interval will be inherently prolonged.

Effects of antipsychotics on QTc[7]				
No effect	**Low effect**	**Moderate effect**	**High effect**	**Unknown effect**
Lurasidone	Aripiprazole Clozapine Flupentixol Olanzapine Paliperidone Risperidone Sulpiride	Amisulpride Chlorpromazine Haloperidol Levomepromazine Quetiapine	Pimozide All antipsychotic doses exceeding the recommended maximum	Trifluoperazine Zuclopenthixol

Monitoring of Antipsychotic Blood Levels

A MHRA drug safety update (August 2020) states that blood level monitoring of antipsychotics for toxicity may be helpful in certain circumstances, where testing and reference values are available[9].

Locally, routine blood level monitoring is not recommended for antipsychotics (excluding Clozapine in certain clinical circumstances). The availability of assays and reference values for other antipsychotics varies; results can take several days to report and reference values are of limited use where they exist.

If toxicity related to antipsychotic medication is suspected, immediate action should be taken in response to the symptoms displayed.

Management of Antipsychotic Induced Weight Gain

A significant proportion of people with diagnosis of severe mental illness develop risk factors for cardiovascular disease and diabetes (smoking, overweight/obesity, alcohol misuse). Factors driving weight gain and the risk of diabetes include: poor lifestyle, effects of antipsychotic treatment (which varies between drugs and which can result in profound weight increase in the first few weeks of treatment), pharmacogenetic differences between individuals and direct effects of some antipsychotic medications to interfere with insulin secretion[10].

Lifestyle interventions should almost always be part of the first line of approach and in most circumstances should be continued alongside any additional intervention. Switching to one of the antipsychotic medications with lower propensity for weight gain is a strategy that should also be considered. This must balance the possible benefit on weight against the risks of inducing relapse of the mental illness.

Metformin can be considered as an adjunct to attenuate or reduce weight gain following antipsychotic medication[8]; prescribing for this indication is Amber 2 classification on the Nottinghamshire Joint Formulary. Lifestyle interventions should have been fully explored and the other interventions considered first. In clinical trials metformin leads to a modest reduction in weight (approximately 2 kg) over the short and long term but is less effective than intensive lifestyle intervention[10]. There are some risks attached to Metformin that require appropriate monitoring (renal function and vitamin B12).

Switching Antipsychotics

Switching from one antipsychotic medication to another requires careful cross titration and should usually be done under specialist supervision. If a patient who is no longer open to mental health services requests a change in antipsychotic, or there are concerns about tolerability or side effects, consider discussing this with the relevant mental health team.

Special Populations

Older People (>65 years)

Due to changes in pharmacokinetics and pharmacodynamics, older people are more susceptible to adverse effects from antipsychotic medication. Consider the need for more frequent reviews of antipsychotic dose, side effects and monitoring requirements (e.g. ECG monitoring). For antipsychotic prescribing in the context of treating behavioural and psychological symptoms of dementia, refer to the appropriate Nottinghamshire APC guidance.

Children and Young People

Oral antipsychotic medication may be prescribed in the context of first episode psychosis, recurrence of psychosis or schizophrenia, psychotic depression, bipolar disorder and as augmentation therapy for obsessive compulsive disorder and body dysmorphic disorder[2,3,5,11].

The choice of antipsychotic medication should be made by the parents or carers of younger children, or jointly with the young person and their parents or carers and healthcare professionals[11]. At the start of treatment, give doses below the lower end of the licensed range for adults if the medication is not licensed for children and young people or at the lower end of the licensed range if the medication is licensed. The dose should be slowly titrated upwards within the dose range given in the BNF, the BNFC or the product SPC[11].

The Child and Adolescent Mental Health Service (CAMHS) should maintain responsibility for monitoring physical health and the effects of antipsychotic medication for at least the first 12 months or until the condition has stabilised. Thereafter, the responsibility for this monitoring may be transferred to primary care. The physical health monitoring requirements for this population are different from the schedule outlined in Appendix two of this guidance. Please see NICE Clinical Guideline 155 or contact the specialist team for more information.

Learning Disability

If antipsychotic medication is prescribed for a mental illness, there is the expectation that the treatment will follow the recommendations of the relevant NICE guidance.

People with a learning disability, autism or both are more likely to be prescribed psychotropic medication (including antipsychotics) than other people. The use of antipsychotic medication in this patient group should be challenged if there is no clear or appropriate indication for the prescription. NICE[12] suggests that specialists consider prescribing antipsychotic medication to manage behaviour that challenges only when:

- Psychological or other interventions alone do not produce change within an agreed time

- Treatment for any coexisting mental or physical health problem has not led to a reduction in the behaviour
- The risk to the person or others is very severe (for example, because of violence, aggression or self-injury)

In all instances of antipsychotic prescribing for behaviour that challenges, regular review is essential and should include a review of effectiveness, side effects and plans for stopping. It is expected that all antipsychotic prescribing for this indication will be short term unless there is a specialist decision to continue based on the following:

- There is evidence that the person with a learning disability, autism or both has gained significant benefit from the use of the antipsychotic and recent attempts to withdraw has resulted in a deterioration
- The nature of the behaviours experienced prior to prescribing the antipsychotic was so severe that withdrawal is considered clinically inappropriate by the carers and others

For more information on reducing the inappropriate prescribing of psychotropic drugs in learning disability, autism or both see:
STOMP - NHS England Information
STOMP – GP prescribing information

Pregnancy and Breastfeeding
Refer to perinatal mental health services for any patient who is taking antipsychotic medication and has a planned or confirmed pregnancy or is breastfeeding.

Discontinuation of Treatment

Acute withdrawal symptoms have been occasionally described after abrupt discontinuation of oral antipsychotics e.g. sweating, insomnia, tremor, anxiety, nausea or vomiting. It is recommended that oral antipsychotics are discontinued gradually, usually over many weeks or months. The risk of relapse on cessation of antipsychotics may be minimised by more gradual tapering.

If a patient has been discharged from mental health services and stops oral antipsychotic medication, primary care is advised to follow up the patient and monitor for signs and symptoms of relapse for at least two years after discontinuation[1]. A re-referral to mental health services should be considered if there are concerns about deterioration in mental state.

Withdrawal symptoms are unlikely following the discontinuation of a depot antipsychotic as blood levels will fall slowly over some weeks after the last injection. If a patient has been discharged from mental health services on depot antipsychotic and expresses a desire to stop their depot (or if they have been stable on the depot for over five years) they should be referred by the GP back to mental health services for advice and assessment.

Contraindications

Refer to the manufacturer's Summary of Product Characteristics (SPC) for the individual product.

Cautions (for all antipsychotics)[13]

Blood dyscrasias, cardiovascular disease, conditions predisposing to seizures, depression, diabetes (may raise blood glucose), epilepsy (may lower seizure threshold), history of jaundice, myasthenia gravis, Parkinson's disease (may be exacerbated), photosensitisation (may occur with higher dosages), prostatic hypertrophy (in adults), severe respiratory disease, susceptibility to angle-closure glaucoma and pregnancy/breastfeeding (refer to the perinatal mental health team).

Refer to the manufacturer's Summary of Product Characteristics (SPC) and BNF for further cautions relevant to the individual product.

Side Effects (for all antipsychotics)[13]

Side effects	Action
Common (≥1% and <10%) or very common (≥10%)	
Extrapyramidal symptoms • Parkinsonism (including joint stiffness and tremor) • Dystonia (abnormal face and body muscle contractions) • Akathisia (restlessness) • Tardive dyskinesia (rhythmic, involuntary movements of tongue, face and jaw)	Parkinsonism: may remit if the dose is reduced or the drug withdrawn. An antimuscarinic (e.g. procyclidine) may be helpful. Dystonia: Dose reduction or an antimuscarinic (e.g. procyclidine) may be helpful. Akathisia: refer to the mental health team. A reduction in dose, discontinuation or change to an alternative atypical antipsychotic maybe required. Tardive Dyskinesia: refer to the mental health team. A reduction in dose, discontinuation or change to an alternative atypical antipsychotic maybe required. Review use of antimuscarinics as these can often worsen Tardive Dyskinesia. Please note that these symptoms can temporarily deteriorate or can even arise after discontinuation of treatment.
Insomnia	Consider dose reduction
Drowsiness	Give as a single night-time dose. Consider temporary dose reduction. Advise patients not to drive/operate machinery if affected
Constipation	High fibre diet, good fluid intake, exercise, laxative.
Dizziness	Give as a single night-time dose. Consider temporary dose reduction. Advise patients to take time to stand up and not to drive/operate machinery if affected.
Raised prolactin (hyperprolactinaemia)	Can be asymptomatic or symptomatic (galactorrhoea, gynaecomastia, disturbances of menstrual cycle/amenorrhoea and sexual dysfunction). Dose-related. Consider dose-reduction or switching to an alternative antipsychotic. Refer to the mental health team.

Hypotension (dose related)	Initiate slowly. Consider dose reduction or dividing the dose.
Weight gain/increased appetite	Encourage a healthy balanced diet and regular exercise. Monitor and refer to a dietician and/or consultant if appropriate. See information above.
QTc interval prolongation	See information in ECG monitoring section above. Monitor and refer to the mental health team as appropriate.
Vomiting	Generally self-limiting. Consider taking after food and/or dividing doses.
Dry mouth	Recommend chewing sugar-free gum. Consider taking after food and/or dividing doses. If severe and persistent consider prescribing artificial saliva.
Arrhythmias and tachycardia	Check pulse, blood pressure and ECG. Refer to the mental health team.
Uncommon (≥ 0.1% and <1%)	
Hyperglycaemia (mostly associated with olanzapine, risperidone, quetiapine and clozapine)	Manage according to local diabetes guidelines. Refer to the mental health team if appropriate.
Blood dyscrasias	Perform blood counts if unexplained infection or fever develops Refer to the mental health team.
Embolism and thrombosis	All possible risk factors for Venous Thromboembolism should be identified before and during antipsychotic treatment and preventative measures undertaken[14]
Neuroleptic Malignant Syndrome (NMS) - hyperthermia, muscle rigidity, autonomic instability, altered consciousness, elevated Creatine Kinase levels	Very rare. Discontinue ALL antipsychotic(s). If suspected immediate referral to an acute hospital is required.

Refer to the manufacturer's Summary of Product Characteristics (SPC) and BNF for further side effects relevant to individual products.

Drug Interactions

Refer to the manufacturer's Summary of Product Characteristics (SPC) and BNF for information on drug interactions.

Patient Information

Patient information leaflets for antipsychotics and mental health conditions can be can be found at:

https://www.choiceandmedication.org/nottinghamshirehealthcare

https://www.rcpsych.ac.uk/mental-health

https://www.mind.org.uk/information-support/a-z-mental-health/

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Mental Health Pharmacy Contacts
Nottinghamshire Healthcare NHS Foundation Trust

Wells Road Centre Pharmacy - 01159 555 356
Highbury Hospital Pharmacy - 0115 854 2247
Millbrook Mental Health Unit Pharmacy - 01159 560 883
Medicines Information Email: MI@nottshc.nhs.uk

Version Control: Antipsychotics - Prescribing Guideline			
Version	Author(s)	Date	Changes
1.0	Hannah Godden, Specialist Mental Health Interface and Efficiencies Pharmacist, Nottingham and Nottinghamshire CCGs/Nottinghamshire Healthcare NHS Foundation Trust John Lawton, Clinical Pharmacy Manager, Nottinghamshire Healthcare NHS Foundation Trust	June 2021	Previous information sheets for second generation (atypical) antipsychotics consolidated into a single document covering all antipsychotics (excluding clozapine)

Appendix One - Criteria for transferring oral and depot antipsychotic prescribing to primary care

- The patient's mental health is stable (this can mean stable but with some residual symptoms)
- The patient is tolerating and accepting a regular dose of antipsychotic medication (or consistently attends for their depot injection)
- If prescribed depot antipsychotic, the patient has been receiving the depot medication for at least 12 months.
- Suitable support arrangements for community care are in place
- An agreed care plan is in place with respect to monitoring the patients' mental and physical health, assessing the effects and side-effects of medication, and actions required if the patient does not collect prescriptions/attend for their depot, shows signs of relapse or intolerable side-effects
- It should be clearly documented in correspondence who will be responsible for prescribing and carrying out the routine monitoring

Mental Health Team Responsibilities

- To assess the patient, establish the diagnosis, determine a management strategy and devise a care plan in conjunction with the GP, other healthcare professionals and appropriate support agencies
- To initiate the antipsychotic medication, titrate to the minimum effective maintenance dose, monitor response and assess/manage initial side-effects
- When prescribing depot antipsychotics to specify the form, strength, dose and dosing interval between injections, and brand where appropriate
- To provide the patient with written information about the illness and the antipsychotic treatment
- To provide primary care with a copy of the agreed care plan
- The care plan should state who is responsible for monitoring the patients mental and physical health at the appropriate time intervals
- To be available for advice and agree an action plan if the GP reports signs of relapse, side-effects, compliance problems or level of risk to self or others is increased
- To have procedures in place for rapid referral by the GP where appropriate
- To prescribe the antipsychotic medication until the GP takes over care
- To notify the GP as soon as practical of any changes to drug treatment or care plan
- For both the GP and the mental health team to receive a copy of any blood test results, the name and address of BOTH parties should be specified on the pathology blood sample form
- To advise on dose adjustments, when it is appropriate to stop and how to stop the antipsychotic medication
- To discharge the patient to primary care when appropriate following agreement with the GP

Primary Care Responsibilities

- To check that the patient engages with the practice and is compliant with oral antipsychotic medication or attends for their antipsychotic depot injection at the agreed times and to follow up the patient in cases of non-attendance

- When prescribing depot antipsychotics to specify the form, strength, dose and dosing interval between injections, and brand where appropriate
- To monitor at regular intervals the mental health, general health and wellbeing of the patient, assess compliance, monitor and manage side-effects, in liaison with the mental health team if necessary
- To ensure the patient has the necessary blood tests and to interpret the results, seeking advice where necessary
- For both the GP and the mental health team to receive a copy of any blood test results, the name and address of BOTH parties should be specified on the pathology blood sample form
- To notify the mental health team as soon as practical of any test results or changes to antipsychotic treatment, if appropriate
- To place the patient on the practice severe mental illness (SMI) register and undertake annual reviews as described above

Patient Responsibilities

- Your mental health team will give you written information about your antipsychotic medication. A good on-line resource is the Royal College of Psychiatrists at http://www.rcpsych.ac.uk/mentalhealthinfoforall.aspx

- If you are unable to attend for your depot injection at the agreed appointment time please could you contact the clinic as soon as possible and make another appointment.

- If you have questions about the possibility of changing your treatment or switching from a depot injection to an oral or tablet preparation, or you are thinking about stopping your treatment, please discuss this first with your GP who can then refer you back to specialist mental health services if necessary.

Appendix Two – Monitoring Requirements for Adults and Older People

General Monitoring Requirements

Ask about compliance and side effects at every consultation.
All patients should be offered an annual physical health check by their GP (more often if clinically indicated). A copy should be sent to the care coordinator and psychiatrist and put in the secondary care notes.

Lifestyle factors	Smoking, alcohol, substance misuse, diet, level of physical activity sexual health, contraceptive advice
Response to treatment	Including changes in symptoms and behaviour
Cardiovascular risk factors	Blood pressure and lipids
Endocrine disorders	Hyperglycaemia/diabetes and hyperprolactinaemia
Other side-effects	Such as weight gain (monitor BMI and waist circumference), sexual dysfunction (check prolactin), lethargy, emergence of extrapyramidal movement disorder side-effects (including tardive dyskinesia)

Schedule for Physical Monitoring[1,2]

	Initial Baseline Health Check (Secondary Care) & During First Year	**Annual Health Check By GP** *(frequency may increase if clinically indicated)*
Thyroid Function	√	√
Liver Function	√	√
Renal Function	√	√ *(dependent upon age)*
Full Blood Count	√	*(only if indicated)*
E.C.G.	√ *(if indicated)*	*(only if indicated – see information above on ECG monitoring)*
Fasting Blood Plasma Glucose and HbA1c	√ *(repeat at 3 months and 12 months)*	√
Weight / Height (B.M.I.) (plotted on chart)	√ *(weekly for 6 weeks and at 3 months and 12 months)*	√
Waist circumference (plotted on chart)	√	√
Lipid Profile	√ *(repeat at 3 months and 12 months)*	√
Pulse and Blood Pressure	√ *(repeat at 3 months and after every dose change)*	√
Prolactin	√	*(only if indicated)*

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Appendix Three - Summary of licensed indications, recommended doses and available products

Drug	Licensed indications and recommended doses	Oral products available - Nottinghamshire Joint Formulary	Additional Information
Amisulpride[1,2]	**Acute and chronic schizophrenic disorders in which positive symptoms and/or negative symptoms are prominent.** **Acute psychotic episodes** Doses between 400-800mg daily in 2 divided doses. Maximum 1200mg daily. **Schizophrenia with predominantly negative symptoms** 50-300mg daily No specific titration is required. For patients with mixed negative and positive symptoms doses should be adjusted to obtain optimal control of positive symptoms. Doses should be reduced in renal impairment - see SPC for further information. Dosage adjustments are not necessary in patients with hepatic impairment.	Generic tablets - 50mg, 100mg, 200mg and 400mg 100mg/ml oral solution sugar-free.	Doses of up to 300mg can be administered once daily. Higher doses should be given twice daily.
Oral Aripiprazole[1,3,4]	**Treatment of schizophrenia in adults** Initially 10–15mg once daily Usual maintenance dose 15mg once daily Maximum dose 30mg once daily **Treatment of moderate to severe manic episodes in Bipolar I Disorder and recurrence prevention of mania in adults** Initially 15mg once daily Maximum dose 30mg once daily Elderly: effectiveness not established in patients over 65 years.	Tablets - 5mg, 10mg, 15mg and 30mg Oro-dispersible tablets - 10mg and 15mg Oral solution 1mg/1mL – very expensive.	The orodispersible tablet should be taken immediately after removal from the blister and placed on the tongue, where it will rapidly disperse in saliva. It may be taken with or without liquid. It may also be dispersed in water.

	Consider lower starting dose (e.g. 5mg once daily) when clinical factors warrant. No dosage adjustment required in renal impairment. No dosage adjustment required in mild-moderate hepatic impairment. Use with caution in severe hepatic impairment – limited experience. The dose may need to be reviewed if co-prescribed with strong CYP3A4/CYP2D6 inhibitors or inducers.	Reserved for initial dose titration in adolescents and in swallowing difficulties where the orodispersible tablet strengths do not meet the required dose.	The aripiprazole orodispersible tablets are bioequivalent to the aripiprazole tablets.
Depot Aripiprazole[1,5]	**Maintenance of schizophrenia in patients stabilised with oral aripiprazole** By deep IM injection: 400mg every month, minimum of 26 days between injections. The dose may need to be reviewed if co-prescribed with strong CYP3A4/CYP2D6 inhibitors or inducers.	Abilify Maintena® 400mg powder and solvent for prolonged-release suspension for injection pre-filled syringes Abilify Maintena® 400mg powder and solvent for prolonged-release suspension for injection vials	Administration into the deltoid or gluteal muscle. Aripiprazole Maintena® requires reconstitution with the solvent provided. Oral aripiprazole should be continued for 14 consecutive days after the first injection whilst blood levels reach steady state.
Chlorpromazine[1,6]	**Schizophrenia and other psychoses, mania and hypomania** Initially 25mg three times daily or 75mg once daily at bedtime. Adjust according to response (usual dose 300mg-600mg per day) Maximum dose 1g daily Use a third to half of usual adult dose in the elderly patients; with a more gradual increase in dosage.	Tablets - 25mg, 50mg and 100mg Oral solution 100mg/5mL and 25mg/5mL	Risk of contact sensitisation - tablets should not be crushed and solutions should be handled with care.

	Start with small doses in severe renal impairment because of increased cerebral sensitivity. Manufacturer advises caution in severe hepatic failure (increased risk of accumulation).		Patients should avoid direct sunlight – risk of photosensitisation.
Clozapine	Refer to the separate Nottinghamshire APC Clozapine Information Sheet		
Oral Flupentixol[1,7]	**Schizophrenia and other psychoses** Initially 3-9mg twice daily, adjusted according to response Maximum dose 18mg daily Elderly: Initially 0.5mg-4.5mg twice daily., adjusted according to response **Depressive illness** Initially 1mg once daily in the morning; increased if necessary to 2mg once daily after 1 week. Doses above 2mg to be given in divided doses, last dose to be taken before 4pm. Maximum 3mg daily Elderly: Use half adult doses Not studied in renal impairment. Start with small doses in severe renal impairment due to increased cerebral sensitivity. Not studied in hepatic impairment but flupentixol is extensively metabolised by the liver; use with extreme caution.	Tablets - 0.5mg, 1mg and 3mg	
Depot Flupentixol decanoate (Depixol® and	**Maintenance in schizophrenia and other psychoses** By deep IM injection Usual maintenance dose 50mg every 4 weeks – 300mg every 2 weeks Maximum dose 400mg per week	Solution for injection 20mg/mL,100mg/mL and 200mg/mL	Administration into the upper outer buttock or lateral thigh

Psytixol®)[1,8]	Elderly: lower doses used		
Oral Haloperidol[1,9]	**Schizophrenia and schizoaffective disorder** 2-10mg daily in 1-2 divided doses. Patients with first episode schizophrenia generally respond to 2-4 mg daily, whereas patients with multiple-episode schizophrenia may need doses up to 10 mg daily. Maximum 20mg daily Elderly: Initially use half the lowest adult dose and adjust gradually according to response up to maximum 5mg daily. Doses >5mg only considered for patients who have tolerated higher doses. **Treatment of mania in bipolar disorder** 2-10mg daily in 1-2 divided doses. Maximum 15mg daily. Elderly: Initially use half the lowest adult dose and adjust gradually according to response up to maximum 5mg daily. Doses >5mg only considered for patients who have tolerated higher doses. **Persistent aggression and psychotic symptoms in moderate-severe Alzheimer's and vascular dementia** Refer to local guidelines Caution advised in renal impairment; in severe impairment consider lower initial dose, adjust the dose in smaller increments and at longer intervals. In hepatic impairment it is recommended to halve the initial dose and then adjust the dose in smaller increments and at longer intervals. A baseline ECG is recommended before treatment	Tablets - 1.5mg, 5mg and 10mg (0.5mg available but very expensive, use liquid if possible) Oral solution 10mg/5mL sugar-free and 5mg/5mL sugar-free	Haloperidol oral solution may be mixed with water to facilitate dose administration, but it must not be mixed with any other liquid. The diluted solution must be taken immediately. Take care not to confuse the different strengths of liquid formulation
Depot Haloperidol	**Maintenance in schizophrenia and schizoaffective disorders** By deep IM injection Usual maintenance dose 50mg-200mg every 4 weeks	Solution for injection 50mg/mL and 100mg/mL	Administration into the gluteal muscle

decanoate (Haldol®)[1,10]	Maximum dose 300mg every 4 weeks Elderly: lower doses used A baseline ECG is recommended before treatment		
Lurasidone[1,11]	**Schizophrenia (adult)** Initially 37 mg once daily, increased if necessary up to 148 mg once daily. **Schizophrenia (when given with moderate CPY3A4 inhibitors e.g. diltiazem, erythromycin, fluconazole and verapamil)** Initially 18.5 mg once daily (max. per dose 74 mg once daily). Dosing recommendations for elderly patients with normal renal function are the same as for adults. In moderate (CrCl ≥30 and <50mL/min), severe (CrCl ≥15 and <30mL/min) and End Stage Renal Disease, the recommended starting dose is 18.5mg once daily, and the recommended maximum dose is 74 mg once daily. In moderate hepatic impairment the starting dose should be 18.5mg once daily and the maximum dose should not exceed 74mg once daily. In severe impairment the starting dose should be 18.5mg once daily and the maximum dose should do not exceed 37mg once daily. Avoid concomitant administration with strong CYP3A4 inhibitors. e.g.clarithromycin, cobicistat, intraconazole, ketoconazole, ritonavir, saquinavir, telithromycin, voriconazole and strong CYP3A4 inducers, e.g. carbamazepine, phenobarbital, phenytoin, rifampicin, St John's wort.	Tablets – 18.5mg, 37mg and 74mg. RED traffic light classification on the Nottinghamshire Joint Formulary	Tablets should be taken with food. If taken without food Lurasidone exposure will likely be significantly lower.
Oral Olanzapine[1, 12, 13]	**Treatment of schizophrenia** Initially 10mg once daily	Tablets - 2.5mg, 5mg, 7.5mg, 10mg,	Oro-dispersible tablets are bio-

	Usual dose 5-20mg daily Maximum 20mg daily **Treatment of mania in Bipolar Disorder** Initially 15mg once daily in monotherapy (10mg once daily in combination therapy). Maximum 20mg daily **Prevention of recurrence in patients with bipolar disorder** Initially 10mg once daily (unless receiving olanzapine therapy for treatment of acute mania then continue the same dose for prophylaxis). Maximum 20mg daily Consider a lower initial dose (2.5mg-5mg/day) for those 65 years of age and older when clinical factors warrant, in patients with hepatic and/or renal impairment and in patients who have multiple factors (female, elderly, non-smoker) that may result in slower metabolism.	15mg and 20mg Orodispersible tablets sugar-free - 5mg, 10mg, 15mg and 20mg	equivalent to standard tablets and should be placed in the mouth or dispersed in a full glass of water or other suitable beverage (e.g. orange / apple juice, milk or coffee) immediately before administration. Oro-dispersible tablets are no faster acting than the standard tablet preparation.
Depot Paliperidone (Xeplion and Trevicta®)[1]	Paliperidone palmitate long-acting intramuscular injection is formulated as a monthly injection (Xeplion®) and a 3-monthly injection (Trevicta®). **Xeplion®** is a monthly injection Maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. Dose at initiation depends on prior treatment. The optimal monthly maintenance dose is 75mg; some patients may benefit from lower or higher doses within the recommended range of 50 to 150mg based on individual patient tolerability and/or efficacy. **Trevicta®** is a 3-monthly injection Maintenance treatment of schizophrenia in adult patients who have been stable on the same monthly dose Xeplion® long-acting	Xeplion® long-acting injection - 50mg, 75mg, 100mg, 150mg Trevicta® long-acting injection - 175mg, 263mg, 350mg, 525mg	Given by deep intramuscular injection into the gluteal or deltoid muscle.

	injection for at least four months. The dose is based on the previous monthly Xeplion® dose.		
Quetiapine[1, 14, 15]	**Treatment of schizophrenia** Immediate release preparations: Day 1: 25mg twice daily, day 2: 50mg twice daily, day 3: 100mg twice daily, day 4: 150mg twice daily Adjust according to response Maximum dose 750mg daily Rate of dose titration may need to be slower and daily dose lower in elderly patients Modified release preparations (adult): Day 1: 300mg once daily, day 2: 600mg once daily Adjust according to response Maximum dose 800mg daily Modified release preparations (elderly): Initially 50mg once daily. Adjust according to response in steps of 50mg daily **Treatment of mania in Bipolar Disorder** Immediate release preparations: Day 1: 50mg twice daily, day 2: 100mg twice daily, day 3: 150mg twice daily, day 4: 200mg twice daily. Adjusted in steps of 200mg daily, according to response Maximum dose 800mg daily Rate of dose titration may need to be slower and daily dose lower in elderly patients Modified release preparations (adult): Day 1: 300mg once daily, day 2: 600mg once daily Adjust according to response Maximum dose 800mg daily	Immediate release tablets - 25mg, 100mg, 150mg, 200mg and 300mg Modified release tablets - 50mg, 150mg, 200mg, 300mg and 400mg Oral solution 20mg/mL	Patients who are being treated with a once-daily dose of a prolonged-release quetiapine tablet may be switched to the equivalent total daily dose of immediate-release quetiapine tablets, taken in one or two divided doses. Once above 300mg/day the immediate release quetiapine should be taken in two divided doses. Can be administered with or without food.

	Modified release preparations (elderly): Initially 50mg once daily. Adjust according to response in steps of 50mg daily **Treatment of depression in Bipolar Disorder** Immediate release preparations: Day 1: 50mg once daily at bedtime, day 2: 100mg once daily, day 3: 200mg once daily, day 4: 300mg once daily. Adjust according to response Maximum dose 600mg daily Rate of dose titration may need to be slower and daily dose lower in elderly patients Modified release preparations: Day 1: 50mg once daily at bedtime, day 2: 100mg once daily, day 3: 200mg once daily, day 4: 300mg once daily. Adjust according to response Maximum dose 600mg daily **Prevention of mania and depression in bipolar disorder** Continue at the dose effective for treatment of bipolar disorder; use lowest effective dose for maintenance therapy **Adjunctive treatment of major depression** Modified release preparations (adult): 50mg once daily at bedtime for 2 days, then 150mg once daily for 2 days. Adjust according to response Usual dose 150-300mg daily No dosage adjustment is required in patients with renal impairment. Quetiapine is extensively metabolised by the liver. Patients with hepatic impairment should be started on 25mg once		

	daily (immediate release) or 50mg once daily (modified release) and gradually increased in 25mg or 50mg steps.		
Oral Risperidone[1, 16]	**Treatment of schizophrenia** Day 1: 2mg daily Day 2: 4mg daily Usual dose 4-6mg daily Higher oral doses (8-16mg/day) may not increase therapeutic benefit and result in more extrapyramidal side effects. Maximum dose is 16mg per day **Treatment of mania in bipolar disorder** Initially 2mg once daily then increased in steps of 1mg daily if required. Usual dose 1-6mg daily A lower starting dose of 250micrograms - 500micrograms twice daily is generally recommended in those over 65 years of age, and those with renal or hepatic disease, gradually increasing to 1-2mg twice daily. **Short term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's disease.** Refer to local guidelines **Short term symptomatic treatment (up to 6 weeks) of persistent aggression in conduct disorder in children from the age of 5 years and adolescents with intellectual disabilities** See BNFC for doses	Tablets – 0.25mg, 0.5mg, 1mg, 2mg, 3mg, 4mg and 6mg. Oral solution 1mg/1mL Oro-dispersible tablets are non-formulary; not cost effective.	Risperidone tablets may be administered once or twice a day. Oro-dispersible and standard tablets are bioequivalent. Oro-dispersible tablets are not faster acting. Can be administered with or without food. The oral liquid may be diluted with any non-alcoholic drink, (except tea).
Depot Risperidone (Risperdal Consta®)[1, 17]	**Schizophrenia and other psychoses in patients tolerant to risperidone by mouth** By deep IM injection Usual maintenance dose 25 – 50mg every two weeks. Maximum 50mg every two weeks.	Risperdal Consta® 25mg, 37.5mg and 50mg powder and solvent for suspension for	Administered into the deltoid or gluteal muscle. The powder must be suspended in the

		injection vials	diluent and administered using the correct size needle provided in the pack. During initiation, oral risperidone should be continued for 4–6 weeks. Must be stored in a refrigerator at between +2 to +8^{0}C. Please contact your local mental health trust pharmacy about temperature excursions.
Sulpiride[1, 18]	**Treatment of schizophrenia with mainly negative symptoms** 200-400mg twice daily Maximum 800mg per day **Treatment of schizophrenia with mainly positive symptoms** 200-400mg twice daily Maximum 2.4g per day Elderly and renal impairment: prescribe lower initial doses and increase gradually. Use with caution in hepatic impairment.	Tablets - 200mg and 400mg Oral solution 200mg/5mL	
Trifluoperazine[1, 19]	**Schizophrenia and other psychoses** Initially 5 mg twice daily, daily dose may be increased to 15 mg after 1 week. If necessary, dose may be further increased in steps of 5 mg at intervals of 3 days. Usually, total daily doses would not exceed 30mg/day. When satisfactory control has been achieved,	Tablets – 1mg and 5mg Oral solution 5mg/5mL	

	reduce gradually until an effective maintenance level has been established. Reduce starting dose in elderly or frail patients by at least half. Renal impairment: Start with small doses in severe renal impairment because of increased cerebral sensitivity. Hepatic impairment: The manufacturer advises to avoid		
Oral Zuclopenthixol[1, 20]	**Treatment of schizophrenia and other psychoses** Initially 20-30mg daily in divided doses Usual maintenance dose 20-50mg daily Maximum dose 150mg daily (maximum 40mg per dose) Elderly: Use lower initial doses (5-15mg daily) and increase gradually. Renal impairment: use half the recommended dose in renal failure and consider using lower initial doses in patients with severe renal impairment. Hepatic impairment: use with caution, consider using half the recommended dose for patients with impaired hepatic function.	Tablets – 2mg, 10mg and 25mg	
Depot Zuclopenthixol decanoate (Clopixol®)[1, 21]	**Maintenance in schizophrenia and paranoid psychoses** By deep IM injection Maintenance dose: 200–500 mg every 1–4 weeks Do not exceed 600mg weekly **Note: Do not confuse the slow and long-acting zuclopenthixol decanoate (Clopixol®, Clopixol Conc®) depot with the faster, shorter-acting zuclopenthixol acetate (Clopixol Acuphase®) formulation which (although not recommended) is used for rapid tranquillisation. Errors have occurred**	Solution for injection 200mg/mL and 500mg/mL	Administered into the upper outer buttock or lateral thigh

	when these products have been interchanged. The drug name and the packaging are very similar.		

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