

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.

Contents

- 1) Therapeutic Summary
- 2) Antipsychotic Initiation
- 3) Depot Antipsychotic Injections
- 4) Duration of Treatment
- 5) Monitoring Requirements and Responsibilities
- 6) ECG Monitoring
- 7) High Dose Antipsychotic Treatment
- 8) Monitoring of Antipsychotic Blood Levels
- 9) Switching Antipsychotics
- 10) Special Populations – Older People
- 11) Special Populations – Children and Young People
- 12) Special Populations – Learning Disability
- 13) Special Populations – Pregnancy and Breastfeeding
- 14) Discontinuation of Treatment
- 15) Contraindications
- 16) Cautions
- 17) Side effects of Antipsychotics
- 18) Management of Antipsychotic Induced Weight Gain
- 19) Management of Hyperprolactinaemia
- 20) Drug Interactions
- 21) Patient Information
- 22) References and Version Control

Appendix 1 - Criteria for Transferring Antipsychotic Prescribing to Primary Care

Appendix 2 - Monitoring Requirements for Adults and Older People

Appendix 3 - Antipsychotic Clinical Information (licensed indications, doses and available products)

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 first episode psychosis or 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 therapy⁴. Modified-release quetiapine is licensed as an adjunct in the treatment of major depression however, this is an off-label use for other antipsychotics. Low dose amisulpride (max. 50mg/day) is an alternative (off-label) to antidepressants for some patients with chronic depression symptoms⁴. A combination of antidepressant and antipsychotic (e.g. olanzapine, quetiapine) is used for depression with psychotic symptoms⁴. Low dose oral flupentixol (up to 3mg/day) is 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 failed⁵.

Antipsychotics may be prescribed for patients with dementia who are experiencing agitation, hallucinations or delusions that are causing them severe distress⁶. 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 unreliable¹.

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 and The British Association for

Psychopharmacology (BAP) 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 on first-generation antipsychotic depots, a longer 2-inch 20g/21g needle should be selected for gluteal administration and a 1.5-inch 22g needle for deltoid administration⁷. Second-generation antipsychotic depots come with their own needles; the manufacturers will provide information on when to use each needle size.

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. 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 years¹. For bipolar disorder treatment should be reviewed within 4 weeks of resolution of symptoms and if continued, reviewed every 3-6 months².

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, initially 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 instances⁸:

- 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 ^{8,9}	
QTc	Action
<440ms (men) or <460ms (women)*	<ul style="list-style-type: none"> • No action required unless other ECG abnormalities
>440ms (men) or >460ms (women) but <500ms**	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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 ⁸				
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 (alone or in combination) exceeding the recommended maximum	Trifluoperazine Zuclopenthixol

High Dose Antipsychotic Treatment

High Dose Antipsychotic Treatment (HDAT) is the use of doses of antipsychotic medication that exceeds the recommended/BNF stated maximum dose. This can be either:

- A single antipsychotic prescribed at dose higher than the BNF recommended maximum; or,
- In combination where more than one antipsychotic is prescribed (including depots), if the combined dose expressed as a percentage is greater than 100%, then the total dose becomes a high dose.

The BNF publishes a maximum recommended dose for each available antipsychotic, however drugs without an official BNF maximum value (e.g., trifluoperazine) are given a notional maximum value consistent with current practice e.g., trifluoperazine 50mg per day.

Prescribers should be aware of the increased incidence of dose-related side-effects, namely extrapyramidal side-effects (EPSEs), sedation, postural hypotension, and anticholinergic effects. HDAT is also associated with ECG changes (particularly QTc prolongation), sudden cardiac death and neuroleptic malignant syndrome (NMS)⁸.

Prescribing at a daily dose higher than the recommended upper limit is outside the manufacturer's product licence i.e., 'off-label prescribing'. HDAT must be an exceptional clinical practice and employed only when standard treatments, including clozapine, have failed. There should be a clear treatment plan in place created by a consultant grade psychiatrist, which includes specific review dates to reduce or switch antipsychotics if HDAT is ineffective.

Due to the increased risks associated with HDAT, the following monitoring guidelines should be taken into consideration¹⁰:

- Baseline physical health investigation to exclude contraindications
- ECG should be repeated 1 month after starting HDAT, and again one month after any subsequent antipsychotic dose increases. If there are no clinical concerns the ECG should be repeated annually.

- Physical observations such as weight/BMI, blood pressure, pulse, and temperature should be monitored and recorded weekly during the first month, then 6 monthly when the treatment is stable.
- Haematological monitoring including U&Es (including eGFR), LFTs, lipids, HbA1c/plasma glucose, and prolactin should be monitored every 6 months.
- Monitor side-effects every 6 months, or one month after any dose changes. Use the Glasgow Antipsychotic Side-effect scale (GASS) or GASS–Clozapine scale where possible.

Where monitoring has been transferred to GP, GPs should continue to complete the annual severe mental illness (SMI) checks which will count towards the HDAT physical observations. Any additional required physical observations should be arranged by the mental health team.

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 available¹¹.

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.

Switching Antipsychotics

Switching from one antipsychotic medication to another requires careful planning 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 or the pharmacy advice line.

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, 3,5,12}.

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 professionals¹¹. 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 SPC¹².

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. NICE¹³ 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 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

Seek advice from the mental health pharmacy advisory line or refer to perinatal mental health services for any patient who is taking antipsychotic medication and has a planned or confirmed pregnancy or is breastfeeding.

Further information is available at:

[Best use of medicines in pregnancy](#)

[e-lactancia](#)

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 discontinuation¹. 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 a 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.

Antipsychotics prescribed for psychoses, bipolar disorder and depression should be stopped by specialist mental health services, or with their advice. The Royal College of Psychiatrists and the charity Mind have patient information guides on their websites covering antipsychotic medicines. If patients are thinking about stopping (or reducing) their antipsychotic medication these guides can provide a helpful framework for a patient discussion. Links: <https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/antipsychotics> ; <https://www.mind.org.uk/information-support/drugs-and-treatments/antipsychotics/about-antipsychotics/>

Antipsychotics are best withdrawn in a gradual tapered fashion over at least 4 weeks, but usually over much longer periods (months, sometimes years) and in proportion to the length of treatment. In high-risk scenarios they may need to be stopped abruptly e.g. following a RED blood test result on clozapine, suspected case of neuroleptic malignant syndrome (NMS).

Contraindications

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

Cautions (for all antipsychotics)¹⁴

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)¹⁴

Side effects	Action
Common ($\geq 1\%$ and $< 10\%$) or very common ($\geq 10\%$)	
Extrapyrasidal symptoms <ul style="list-style-type: none"> • 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. See information below on management of hyperprolactinaemia.
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 consider seeking advice from the mental health pharmacy advisory line.
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.
Hyperglycaemia (mostly associated with olanzapine, risperidone, quetiapine and clozapine)	Manage according to local diabetes guidelines. Refer to the mental health team if appropriate.
Uncommon ($\geq 0.1\%$ and $<1\%$)	
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 ¹⁶
Neuroleptic Malignant Syndrome (NMS) - hyperthermia, muscle rigidity, autonomic instability, altered consciousness, elevated Creatine Kinase levels	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.

If there are questions or concerns around side-effects, consider seeking advice from the pharmacy advice line.

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 secretion¹⁵.

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 medication⁸; 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 intervention¹⁵. There are some risks attached to metformin that require appropriate monitoring (renal function and vitamin B12).

Management of Hyperprolactinaemia⁸

Individual antipsychotics are associated with varying risk of increased prolactin levels.

Prolactin sparing (Prolactin increase very rare)	Low risk of prolactin increase	High risk of prolactin increase
Aripiprazole	Lurasidone	Amisulpride
Clozapine	Olanzapine	Chlorpromazine
Quetiapine		Flupentixol
		Haloperidol
		Paliperidone
		Risperidone
		Sulpiride
		Trifluoperazine
		Zuclopenthixol

Prolactin should be checked at baseline and then annually if indicated. This would include if a patient were reporting symptoms of hyperprolactinaemia (sexual dysfunction, menstrual disturbances, breast growth and galactorrhoea) or if the patient were prescribed an antipsychotic with a high risk of prolactin increase.

The management of hyperprolactinaemia depends mostly on symptoms and long-term risk rather than the reported plasma prolactin level. In the event of an elevated prolactin level (530 – 2500mIU/L):

- Assess for prolactin-related side effects and discuss with the patient clinical consequences of prolonged raised prolactin levels.
- If the patient is asymptomatic take a joint decision on whether to continue the current treatment with annual monitoring, reduce the antipsychotic dose, or switch to an alternative antipsychotic.
- If the patient is symptomatic, consider reducing the antipsychotic dose or switching to an alternative antipsychotic.

A highly elevated prolactin level (>2500mIU/L) should be further investigated to rule out prolactinoma.

Note that prolactin can also be raised due to stress, pregnancy and lactation, renal impairment and other medical conditions. The blood sample for prolactin should ideally be taken early in the morning and stress during venepuncture should be minimised.

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 found at:

<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

Mental Health Pharmacy Advisory Line - 0300 303 5808

Wells Road Centre Pharmacy - 01159 555 356

Medicines Information Email: MI@nottshc.nhs.uk

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
- 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 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 medication
- 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, including suspected or confirmed non-compliance, if appropriate
- To place the patient on the practice SMI register and undertake annual reviews as described above
- To refer back to the mental health team for advice if considering treatment discontinuation

Patient Responsibilities

- Your mental health team will give you written information about your antipsychotic medication. A good online 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		
<p><i>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.</i></p>		
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	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 <i>(frequency may increase if clinically indicated)</i>
Thyroid Function	√	√
Liver Function	√	√
Renal Function	√	√ <i>(dependent upon age)</i>
Full Blood Count	√	<i>(only if indicated)</i>
E.C.G.	√ <i>(if indicated)</i>	<i>(only if indicated – see information above on ECG monitoring)</i>
Fasting Blood Plasma Glucose and HbA1c	√ <i>(repeat at 3 months and 12 months)</i>	√
Weight / Height (B.M.I.) (plotted on chart)	√ <i>(weekly for 6 weeks and at 3 months and 12 months)</i>	√
Waist circumference (plotted on chart)	√	√
Lipid Profile	√ <i>(repeat at 3 months and 12 months)</i>	√
Pulse and Blood Pressure	√ <i>(repeat at 3 months and after every dose change)</i>	√
Prolactin	√	<i>(only if indicated)</i>

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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}	<p>Acute and chronic schizophrenic disorders in which positive symptoms and/or negative symptoms are prominent.</p> <p>Acute psychotic episodes Doses between 400-800mg daily in 2 divided doses. Maximum 1200mg daily.</p> <p>Schizophrenia with predominantly negative symptoms 50-300mg daily</p> <p>No specific titration is required. For patients with mixed negative and positive symptoms doses should be adjusted to obtain optimal control of positive symptoms.</p> <p>Doses should be reduced in renal impairment - see SPC for further information. Dosage adjustments are not necessary in patients with hepatic impairment.</p>	<p>Generic tablets - 50mg, 100mg, 200mg and 400mg</p> <p>100mg/ml oral solution sugar-free.</p>	<p>Doses of up to 300mg can be administered once daily. Higher doses should be given twice daily.</p> <p>Low dose amisulpride (max. 50mg/day) can be used off-label for patients with chronic depression symptoms that have not responded to SSRIs or SNRIs³⁰.</p>
Oral Aripiprazole^{1,3-7}	<p>Treatment of schizophrenia Initially 10–15mg once daily Usual maintenance dose 15mg once daily Maximum dose 30mg once daily</p> <p>Treatment and recurrence prevention of mania in bipolar disorders as per NICE CG185 Initially 15mg once daily Maximum dose 30mg once daily</p> <p>Elderly: effectiveness not established in patients over 65 years. Consider lower starting dose (e.g. 5mg once daily) when clinical factors warrant.</p> <p>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.</p> <p>The dose may need to be reviewed if co-prescribed with strong CYP3A4/CYP2D6 inhibitors or inducers.</p>	<p>Tablets - 5mg, 10mg, 15mg and 30mg</p> <p>Oro-dispersible tablets - 10mg and 15mg</p> <p>Oral solution 1mg/1mL – very expensive. Reserved for initial dose titration in adolescents and in swallowing difficulties where the orodispersible tablet strengths do not meet the required dose.</p>	<p>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.</p> <p>The aripiprazole orodispersible tablets are bioequivalent to the aripiprazole tablets.</p> <p>Aripiprazole can be used off-label to augment antidepressants in treatment resistant depression³⁰. The usual dose range is 2-20mg/day³¹.</p>
Depot Aripiprazole^{1,8}	<p>Maintenance of schizophrenia in patients stabilised with oral aripiprazole By deep IM injection: 400mg every month, minimum of 26 days between injections.</p> <p>The dose may need to be reviewed if co-prescribed with strong CYP3A4/CYP2D6 inhibitors or inducers.</p>	<p>Abilify Maintena[®] 400mg powder and solvent for prolonged-release suspension for injection <u>pre-filled syringes</u></p>	<p>Administration into the deltoid or gluteal muscle.</p> <p>Aripiprazole Maintena[®] requires reconstitution with the solvent provided.</p>

		Abilify Maintena® 400mg powder and solvent for prolonged-release suspension for injection <u>vials</u>	Aripiprazole Maintena® can be loaded with either 14 days of oral aripiprazole after the first injection, or with two 400mg injections at different sites on the same day, along with a single 20mg dose of oral aripiprazole.
Chlorpromazine ^{1,9}	<p>Schizophrenia and other psychoses, mania and hypomania Initially 25mg three times daily or 75mg once daily at bedtime. Adjust according to response (usual dose 75mg-300mg per day) Maximum dose 1g daily</p> <p>Use a third to half of usual adult dose in the elderly patients; with a more gradual increase in dosage.</p> <p>Start with small doses in severe renal impairment because of increased cerebral sensitivity. Manufacturer advises caution in severe hepatic failure (increased risk of accumulation).</p>	<p>Tablets - 25mg, 50mg and 100mg</p> <p>Oral solution 100mg/5mL and 25mg/5mL</p>	<p>Risk of contact sensitisation - tablets should not be crushed and solutions should be handled with care.</p> <p>Patients should avoid direct sunlight – risk of photosensitisation.</p>
Clozapine	Refer to the separate Nottinghamshire APC Clozapine Information Sheet		
Oral Flupentixol ^{1,10}	<p>Schizophrenia and other psychoses Initially 3-9mg twice daily, adjusted according to response Maximum dose 18mg daily</p> <p>Elderly: Initially 0.75mg-4.5mg twice daily., adjusted according to response</p> <p>Depressive illness³² 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 Rarely used for depression indication Not studied in renal impairment. Start with small doses in severe renal impairment due to increased cerebral sensitivity.</p> <p>Not studied in hepatic impairment but flupentixol is extensively metabolised by the liver; use with extreme caution.</p>	Tablets - 0.5mg, 1mg and 3mg	
Depot Flupentixol decanoate (Depixol® and Psytixol®) ^{1,5,11}	<p>Maintenance in schizophrenia and other psychoses By deep IM injection Test dose 20mg, then 20-40mg after at least 7 days, then 20-40mg every 2-4 weeks. Usual maintenance dose 50mg every 4 weeks – 300mg every 2 weeks Maximum dose 400mg per week</p> <p>Elderly: dose is initially quarter to half of adult dose</p>	Solution for injection 20mg/mL, 100mg/mL and 200mg/mL	<p>Administration into the upper outer buttock or lateral thigh</p> <p>The base is thin vegetable oil derived from coconuts. Some patients may have an allergy to this.</p>
Oral Haloperidol ^{1,7,12}	Schizophrenia and schizoaffective disorder	Tablets – 1.5mg, 5mg and 10mg (0.5mg available but	Haloperidol oral solution may be mixed with water to

	<p>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</p> <p>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.</p> <p>Treatment of mania in bipolar disorder 2-10mg daily in 1-2 divided doses. Maximum 15mg daily.</p> <p>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.</p> <p>Persistent aggression and psychotic symptoms in moderate-severe Alzheimer's and vascular dementia Refer to local guidelines</p> <p>Caution advised in renal impairment; in severe impairment consider lower initial dose, adjust the dose in smaller increments and at longer intervals.</p> <p>In hepatic impairment it is recommended to halve the initial dose and then adjust the dose in smaller increments and at longer intervals.</p> <p>A baseline ECG is recommended before treatment</p>	<p>very expensive, use liquid if possible)</p> <p>Oral solution 10mg/5mL sugar-free and 5mg/5mL sugar-free</p>	<p>facilitate dose administration, but it must not be mixed with any other liquid. The diluted solution must be taken immediately.</p> <p>Take care not to confuse the different strengths of liquid formulation</p>
<p>Depot Haloperidol decanoate (Haldol®)^{1,13}</p>	<p>Maintenance in schizophrenia and schizoaffective disorders [in patients currently stabilised on oral haloperidol] By deep IM injection Initially 25-150mg every 4 weeks, adjusted in steps of up to 50mg every 4 weeks Usual maintenance dose 50mg-200mg every 4 weeks Maximum dose 300mg every 4 weeks</p> <p>Elderly: Initially 12.5-25mg every 4 weeks, increased to 25-75mg every 4 weeks. Doses above 75mg every 4 weeks should only be considered for patients who have tolerated high doses</p> <p>A baseline ECG is recommended before treatment</p>	<p>Solution for injection 50mg/mL and 100mg/mL</p>	<p>Administration into the gluteal muscle</p> <p>The base is sesame oil. Some patients may have an allergy to this.</p>
<p>Lurasidone^{1,14}</p>	<p>Schizophrenia (adult) Initially 37 mg once daily, increased if necessary up to 148 mg once daily.</p> <p>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).</p> <p>Dosing recommendations for elderly patients with normal renal function are the same as for adults.</p>	<p>Tablets – 18.5mg, 37mg and 74mg.</p>	<p>Tablets should be taken with food. If taken without food Lurasidone exposure will likely be significantly lower.</p>

	<p>In moderate (CrCl ≥ 30 and < 50 mL/min), severe (CrCl ≥ 15 and < 30 mL/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.</p> <p>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.</p> <p>Avoid concomitant administration with strong CYP3A4 inhibitors. e.g. clarithromycin, cobicistat, itraconazole, ketoconazole, ritonavir, saquinavir, telithromycin, voriconazole and strong CYP3A4 inducers, e.g. carbamazepine, phenobarbital, phenytoin, rifampicin, St John's wort.</p>		
Oral Olanzapine ^{1,6,7,15,16}	<p>Treatment of schizophrenia Initially 10mg once daily Usual dose 5-20mg daily Maximum 20mg daily</p> <p>Treatment of mania in bipolar disorder Initially 15mg once daily in monotherapy (10mg once daily in combination therapy). Usual dose 5-20mg daily Maximum 20mg daily</p> <p>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). Usual dose 5-20mg daily Maximum 20mg daily</p> <p>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.</p>	<p>Tablets – 2.5mg, 5mg, 7.5mg, 10mg, 15mg and 20mg</p> <p>Orodispersible tablets sugar-free – 5mg, 10mg, 15mg and 20mg</p>	<p>Oro-dispersible tablets are bio-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.</p> <p>Oro-dispersible tablets are no faster acting than the standard tablet preparation.</p> <p>Olanzapine can be used off-label to augment antidepressants in treatment resistant depression^{30,31}.</p>
Depot Paliperidone ^{1, 17-20}	<p>Paliperidone palmitate long-acting intramuscular injection is formulated as a monthly injection (Xeplion® or Paliperidone TEVA), a 3-monthly injection (Trevicta®), and a 6-monthly injection (Byanlli®).</p> <p>Xeplion® and Paliperidone TEVA are equivalent. They are given as 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.</p>	<p>Xeplion® long-acting injection – 50mg, 75mg, 100mg, 150mg</p> <p>Paliperidone TEVA long-acting injection – 50mg, 75mg, 100mg, 150mg.</p> <p>Trevicta® long-acting injection – 175mg, 263mg, 350mg, 525mg</p>	<p>Given by deep intramuscular injection into the gluteal or deltoid muscle.</p> <p>Monthly paliperidone palmitate requires a loading dose of 150mg on day 1, followed by 100mg on day 8, followed by the maintenance dose one month after the day 8 injection.</p>

	<p>Trevicta® is a 3-monthly injection (RED status on Joint Formulary) Maintenance treatment of schizophrenia in adult patients who have been stable on the same monthly dose of paliperidone long-acting injection for at least six months. The dose is based on the previous monthly dose.</p> <p>Byanlli® is a 6-monthly injection (RED status on Joint Formulary)</p> <p>Maintenance treatment of schizophrenia in adult patients who have been stable on the same 3-monthly dose of Trevicta® for at least 4 injections.</p>	Byanlli® - 700mg and 1000mg	
Quetiapine ^{1,7,21,22}	<p>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, then adjust according to response Maximum dose 750mg daily Rate of dose titration may need to be slower and daily dose lower in elderly patients</p> <p>Modified release preparations (adult): Day 1: 300mg once daily, day 2: 600mg once daily Adjust according to response Maximum dose 800mg daily</p> <p>Modified release preparations (elderly): Initially 50mg once daily. Adjust according to response in steps of 50mg daily</p> <p>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, then adjusted in steps of up to 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</p> <p>Modified release preparations (adult): Day 1: 300mg once daily, day 2: 600mg once daily Adjust according to response Maximum dose 800mg daily</p> <p>Modified release preparations (elderly): Initially 50mg once daily. Adjust according to response in steps of 50mg daily</p> <p>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, then adjust according to response</p>	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.

	<p>Maximum dose 600mg daily Rate of dose titration may need to be slower and daily dose lower in elderly patients</p> <p>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, then adjust according to response Maximum dose 600mg daily</p> <p>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</p> <p>Adjunctive treatment of major depression Modified release preparations (adult): 50mg once daily at bedtime for 2 days, then 150mg once daily for 2 days, then adjust according to response Usual dose 150-300mg daily</p> <p>Modified release preparations (elderly): 50mg once daily for 3 days, then 100mg once daily for 4 days, then adjust in steps of 50mg. Usual dose 50-300mg daily Dose of 300mg should not be reached before day 22 of treatment</p> <p>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.</p>		
<p>Oral Risperidone^{1,7,23,24}</p>	<p>Acute and chronic psychosis 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</p> <p>Elderly: Initially 0.5mg twice daily, then increased in steps of 0.5mg twice daily. Usual dose 1-2mg twice daily</p> <p>Treatment of mania in bipolar disorder Initially 2mg once daily then increased in steps of 1mg daily if required. Usual dose 1-6mg daily</p> <p>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.</p>	<p>Tablets – 0.25mg, 0.5mg, 1mg, 2mg, 3mg, 4mg and 6mg.</p> <p>Oral solution 1mg/1mL</p> <p>Oro-dispersible tablets are non-formulary; not cost effective.</p>	<p>Risperidone tablets may be administered once or twice a day.</p> <p>Oro-dispersible and standard tablets are bioequivalent.</p> <p>Oro-dispersible tablets are not faster acting.</p> <p>Can be administered with or without food.</p> <p>The oral liquid may be diluted with any non-alcoholic drink, (except tea).</p>

	<p>Short term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's disease. Refer to local guidelines</p> <p>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</p>		<p>Risperidone can be used off-label to augment antidepressants in treatment resistant depression³⁰. The usual dose range is 0.5-3mg/day³¹.</p>
Sulpiride ^{1,26}	<p>Treatment of schizophrenia with mainly negative symptoms 200-400mg twice daily Maximum 800mg per day</p> <p>Treatment of schizophrenia with mainly positive symptoms 200-400mg twice daily Maximum 2.4g per day</p> <p>Elderly and renal impairment: prescribe lower initial doses and increase gradually. Use with caution in hepatic impairment.</p>	<p>Tablets – 200mg and 400mg</p> <p>Oral solution 200mg/5mL</p>	
Trifluoperazine ^{1,27}	<p>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, reduce gradually until an effective maintenance level has been established.</p> <p>Reduce starting dose in elderly or frail patients by at least half.</p> <p>Renal impairment: Start with small doses in severe renal impairment because of increased cerebral sensitivity.</p> <p>Hepatic impairment: The manufacturer advises to avoid</p>	<p>Tablets – 1mg and 5mg</p> <p>Oral solution 5mg/5mL</p>	<p>There is no BNF maximum licensed dose. 50mg daily is used as a maximum dose by convention.</p>
Oral Zuclopenthixol ^{1,28}	<p>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)</p> <p>Elderly: Use lower initial doses (5-15mg daily) and increase gradually.</p> <p>Renal impairment: use half the recommended dose in renal failure and consider using lower initial doses in patients with severe renal impairment.</p> <p>Hepatic impairment: use with caution, consider using half the recommended dose for patients with impaired hepatic function.</p>	<p>Tablets – 2mg, 10mg and 25mg</p>	
Depot Zuclopenthixol decanoate (Clopixol®) ^{1,5,29}	<p>Maintenance in schizophrenia and paranoid psychoses By deep IM injection</p>	<p>Solution for injection 200mg/mL and 500mg/mL</p>	<p>Administered into the upper outer buttock or lateral thigh</p>

	<p>Test dose 100mg, followed by 200-500mg after at least 7 days. Maintenance dose: 200–500 mg every 1–4 weeks Do not exceed 600mg weekly</p> <p>Elderly: a quarter to half usual stating dose to be used</p> <p>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 when these products have been interchanged. The drug name and the packaging are very similar.</p>		<p>The base is thin vegetable oil derived from coconuts. Some patients may have an allergy to this.</p>
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