Derbyshire Healthcare
NHS Foundation Trust

DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Antipsychotic Prescribing and Management for mental health conditions

Antipsychotic medicines feature in the treatment of a wide range of conditions and a number of national guidelines. All antipsychotic medicines are cost-effective treatments when used appropriately and in-line with clinical evidence. Choice of antipsychotic is largely driven by the acceptability of each specific medicine to the patient; with an acceptable range of side effects often being of greater importance than the objective level of symptom reduction.

This document:

- Provides a brief "one stop" summary of recommended antipsychotic use in the context of treating mental health conditions, incorporating Derbyshire Joint Area Prescribing Committee (JAPC) formulary decisions and
- indicates and reminds where agreed guidance on the monitoring of the physical health of patients who are prescribed antipsychotics applies, meaning that specialist services who initiate antipsychotics must retain responsibility for monitoring the patient for at least the first 12-months of their treatment

Antipsychotic use in patients aged 17 or under

Prescribing of antipsychotic medication to children and adolescents is occasionally required. Such prescribing will be initiated and maintained in secondary care, along with any medication-specific physical health monitoring.

Document Updates	Date Updated
Appendix 3 p10 links to SPS updated	October 2024

Content

1. Oral antipsychotics for psychosis

A broad range of oral antipsychotics will be retained in a 1st/2nd line capacity for prescribing in the context of psychosis, including schizophrenia and schizoaffective disorder but encompassing a wide range of related diagnoses. Use of these medicines is likely to be long-term for the majority of patients and cardiometabolic ("Lester") monitoring[1] is required.

A smaller range of medicines will be restricted to a specific second-line formulary category, usually associated with newer medicines (including "back triangle" medicines) or those prescribed to specific cohorts of patients. The status of these medicines will be reviewed in the light of clinical experience.

Clozapine will be retained as a 3rd-line agent for "treatment-resistant" patients and will remain a "red" drug for specialist prescribing and monitoring.

There is also a 4th-line category for treatments prescribed when clozapine is indicated but either ineffective or not tolerated. This includes scenarios such as prescribing antipsychotics at doses in excess of BNF maxima (either alone or in combination).

Table 1: Oral antipsychotic medicines for psychosis

	Medicine	Notes	Traffic-light status
1st/2nd line	Amisulpride		Green with specialist initiation, in line with Derbyshire prescribing specification Secondary care will monitor for 1 year minimum in line with physical monitoring guideline – appendix 3 (mandatory)
	Aripiprazole		
	Chlorpromazine		
	Flupentixol		
	Haloperidol		
	Olanzapine		
	Quetiapine		
	Risperidone		
	Sulpiride		
	Trifluoperazine		
	Zuclopenthixol		
2nd line only	Cariprazine[2]	Only after an adequate trial of aripiprazole (unless contraindicated)	Red
	Lurasidone	e.g. for patients with a history of metabolic syndrome or where this is a specific concern pre-treatment and aripiprazole has been ineffective, not tolerated or is contra-indicated	
3rd Line	Clozapine	For treatment resistance and for Parkinson's Disease Psychosis	Red
4th Line	Antipsychotic polypharmacy (other than cross-tapering or adjunctive aripiprazole for hyperprolactinaemia[3])	For treatment resistant cases where clozapine is not effective or not tolerated	Red
	High-dose antipsychotic regimens		

[1] ncap-e-version-nice-endorsed-lester-uk-adaptation.pdf (rcpsych.ac.uk)
[2] Women of childbearing potential must use highly effective contraception while taking cariprazine and at least for 10 weeks after stopping treatment. Women using systemically acting hormonal contraceptives should add a second (barrier) method.
[3] Aripiprazole is an evidenced-based adjunctive option to reduce antipsychotic-induced hyperprolactinaemia (unlicensed indication)

2. Oral antipsychotics for bipolar affective disorder

The range of oral antipsychotics to be used to treat bipolar affective disorder is narrower than that for psychosis, led by NICE CG185 (2014) and evidence that has emerged subsequently. NICE-recommended medicines provide clear 1st/2nd line options, supported by specific choices for cases where these have proven unhelpful and the evidence suggests potential for benefit.

The use of antipsychotic medication for bipolar affective disorder is likely to be for the medium- to long-term. Lester monitoring is appropriate to this use of antipsychotic medication.

Table 2: Oral antipsychotics for bipolar disorder

	Medicine	Notes	Traffic-light status
1st/2nd line	Aripiprazole	Recommended options in NICE CG 185	Green with specialist initiation, in line with Derbyshire prescribing specification Secondary care will monitor for 1 year minimum in line with physical monitoring guideline – appendix 3 (mandatory)
	Haloperidol		
	Olanzapine		
	Quetiapine		
	Risperidone		
Specialist use only	Clozapine	For treatment-resistance	Red
	Lurasidone	For bipolar depression	Red

3. Oral antipsychotics for anxiety disorders

Antipsychotics are not a first-line pharmacological treatment for anxiety disorders. They may occasionally be initiated by specialists for patients who have not responded to other interventions. Such use is likely to be "off-label" and as augmentation of other medicines. Choice of antipsychotic will be guided by the available guidance from NICE for the specific anxiety disorder, supplemented where necessary by other consensus guidance such as that published by the British Association for Psychopharmacology and the research literature. The evidence base is not strong enough to make definitive formulary statements about the choice of antipsychotic when treating anxiety disorders requiring intensive interventions.

From a formulary viewpoint, the treatment of anxiety disorders is not expected to include any antipsychotic medicine not already allocated a traffic light status for psychosis and physical health monitoring responsibility will follow the same expectations.

4. Oral antipsychotics for treatment of depression

Some oral antipsychotic medication may be prescribed in the context of depression as a regular adjunct to antidepressant medication when the antidepressant alone has not proven sufficiently effective. Oral antipsychotic medication may also be prescribed in addition to an antidepressant for people experiencing psychotic depression and may be continued for a number of months after remission of psychotic symptoms. A summary is provided in Table 3, covering the 1st and 2nd line adjunctive options but not precluding other antipsychotics being used for this purpose where initial options are ineffective, contra-indicated or not tolerated.

As these uses are likely to be for the medium-term at least, it is pragmatic to include this cohort of patients in Lester monitoring. Should ongoing prescribing not be necessary then this monitoring can of course be ceased.

Table 3: Antipsychotics as an adjunct to antidepressant treatment in unipolar depression

	Medicine	Notes	Traffic-light status
1st/2nd line as adjunct to antidepressant	Aripiprazole		Green with specialist initiation, in line with Derbyshire prescribing specification Secondary care will monitor for 1 year minimum in line with physical monitoring guideline – appendix 3 (mandatory)
	Olanzapine		
	Quetiapine		
	Risperidone		
1st/2nd line as adjunct in psychotic depression	Olanzapine		
	Quetiapine		

Amisulpride may be prescribed at low doses as a further-line treatment for chronic depressive symptoms (see NICE NG222 [2022]). Because only low doses are used the physical monitoring guideline for antipsychotics does not apply.

	Medicine	Notes	Traffic-light status
As antidepressant monotherapy following specialist initiation for chronic depression	Amisulpride	Unlicensed indication, NICE recommended. Dose not to exceed 50mg daily as higher doses may worsen depression and increase risk of side-effects	Green with specialist recommendation, in line with Derbyshire prescribing specification

5. Oral antipsychotics for the short-term management of non-cognitive symptoms in dementia

Oral antipsychotics are an option to be used with due care and consideration in the treatment of non-cognitive symptoms of dementia where people are at risk of harming themselves or are experiencing agitation, hallucinations or delusions that are causing severe distress. The lowest possible dose should be used for the shortest possible time. The person should be reassessed every 6 weeks to check whether they still require the medication. For more details see NICE NG97 and the JAPC guidance on management of non-cognitive symptoms of dementia.

LESTER monitoring recommendations are not indicated in this situation.

A summary of the antipsychotic options and their management is provided in table 4:

Table 4: Oral antipsychotics in the management of non-cognitive symptoms of dementia

	Medicine	Notes	Traffic-light status
1st Line	Haloperidol		Green for this indication
	Risperidone		
2nd Line	Aripiprazole		Green for this indication with specialist recommendation[4]
	Olanzapine		
	Quetiapine		

[4] This does not preclude short-term prescribing being provided by specialists, such as in Dementia Rapid Response Teams

6. Depot and long-acting injectable antipsychotics

These products offer a consistency of medicines administration that can be beneficial to some patients who require long-term antipsychotic treatment. Despite a higher average acquisition cost than oral antipsychotic medicines they are cost effective and associated with lower rates of relapse and hospitalisation than oral antipsychotics other than clozapine.

Table 5: Depot and long-acting injectable antipsychotics

	Medicine	Notes	Traffic-light status
1st/2nd Line	Flupentixol decanoate	1st generation antipsychotics	Red
	Haloperidol decanoate		
	Zuclopenthixol decanoate		
	Aripiprazole	2nd generation "atypical" antipsychotics	
	Paliperidone (Xeplion®)		
	Risperidone (Risperdal Consta®)		
	Olanzapine embonate	2nd generation antipsychotic that requires administration in a medical facility	Red

Zuclopenthixol acetate

Zuclopenthixol acetate, also known by the brand name (Clopixol Acuphase) is an injectable formulation of zuclopenthixol with an intermediate onset and duration of effect. It is used occasionally in the acute treatment of psychosis only in mental health inpatient environments, in accordance with DHCFT clinical guidelines. It is a **Red** drug within Derbyshire.

Healthcare professionals should remain alert to the risk of erroneous prescribing of this product due to confusion with the longer acting depot formulations of zuclopenthixol decanoate.

Appendix 1- Antipsychotic prescribing for antisocial personality disorder and borderline personality disorder

For the short-term management of crisis in patients with these diagnoses, antipsychotics are regarded as Red drugs and that prescribing is managed by the specialist team.

For the longer-term treatment of a stated comorbid condition the selection, sequencing and monitoring of antipsychotic medicines should be guided by the relevant pathway for the comorbid condition (e.g. psychosis, bipolar disorder), including the sequencing of formulary choices, the application of traffic light categorisation and the completion of Lester physical health monitoring and intervention.

Best practice when prescribing medication in personality disorder (not specific to antipsychotics)

The following have been adapted with permission from the Northumberland Tyne and Wear NHS Foundation Trust Good Practice Guideline on Prescribing Medication and the Personality Disorder Pathway (2017):

Fundamental Guiding Principles

- There are no licensed medicines for use in the management of PD
- Medicines have a role to play in treating co-morbid conditions and these should be prescribed within the appropriate NICE condition guideline and any local clinical guidelines (e.g. antipsychotic physical health monitoring)
- Psychotropic medicines may be useful in the short-term management of a crisis but should be discontinued within 1 week once the crisis has resolved
- Since assessments of PD are often imprecise or unstructured and comorbid conditions are difficult to distinguish, it is best to start with psychosocial management and treatment, and review the symptom/problem profile and formulation at the earliest opportunity
- Some clients put pressure on clinicians to prescribe in order to feel “heard” or “taken seriously”. Best practice would be to tolerate this pressure, validate the client’s need or feelings, and explain the limits of prescribing and the alternatives available (psychosocial treatments)
- A crisis plan should refer to how crises will be managed including the role of hospital admission and prescribing expectations that are realistic.
- A full explanation of the reasons for medication being prescribed should be documented and how this will be reviewed in the context of the overall care plan.

Managing the Client’s expectations

Where there is a request from the client and/or the carer or family member to provide medication and this may not appear indicated, the following guidance is recommended:

- Provide information about the evidence-base for medication in the treatment and management of personality and other problems, as applicable
- Validate (express the positive value of) the client’s needs or feelings behind the request in a non-judgemental and compassionate way
- Identify how the evidence base supports the use of psychosocial approaches and how these underpin the current care plan
- Say no to the request if this is indicated but balance this with a positive statement about the client’s autonomy and role in their care plan and recovery
- Suggest linking up with the care coordinator to review their expectations from treatment and their treatment goals if needed
- Offer to see and review them again if they wish

Before starting short-term drug treatments for people with borderline PD during a crisis:

- Ensure there is consensus among prescribers and other involved professionals about the drug used and that the primary prescriber is identified
- Establish the likely risks of prescribing, including alcohol and illicit drug use
- Briefly discuss the risks of iatrogenic harm and dependency which may arise through the inappropriate use of medication

- Take account of the psychological role of prescribing (both for the individual and the prescriber) and the impact that prescribing decisions may have on the therapeutic relationship and the overall care plan, including long-term treatment strategies
- Ensure that a drug is not used in place of other more appropriate interventions
- Use a single drug
- Avoid polypharmacy wherever possible

When prescribing short-term drug treatment for people with borderline PD in a crisis:

- Choose a drug that has a low side-effect profile, low addictive properties, minimum potential for misuse and relative safety in overdose
- Use the minimum effective dose
- Prescribe fewer tablets more frequently if there is a significant risk of overdose
- Agree with the client the target symptoms, monitoring arrangements and anticipated duration of treatment
- Agree with client a plan for adherence
- Discontinue the drug after a trial period of the target symptoms do not improve (maximum of one week) of if it is not tolerated or felt to be beneficial and the patient requests it to be stopped
- Consider alternative treatments including psychological treatments if target symptoms do not improve or the level of risk does not diminish
- Consider the use of a "contract" outlining that the prescription is for a 1-week period only and the reason for this, and the reasons for stopping it as outlined above
- Arrange an appointment to review the overall care plan, including pharmacological and other treatments, after the crisis has subsided.

After a crisis has resolved or subsided ensure that crisis plans and, if necessary, the overall care plan are updated as soon as possible to reflect current concerns and identify which treatment strategies have proved helpful. The review should include:

- A **review of drug treatment**, including benefits, side effects, any safety concerns and role in the overall treatment strategy
- A documented plan to **stop drug treatment begun during a crisis**, usually within 1 week; if the drug treatment started during a crisis cannot be stopped within 1-week there should be a regular review of the drug to monitor effectiveness, side-effects, misuse and dependency. The frequency of the review should be agreed with the client and recorded in the overall care plan

What are the risks of prescribing medication when it is not recommended or indicated for the client?

1. **Dependency and preventing recovery**: the client may feel that they "need" medication on order to help them recover, so they become more and more dependent on it. This may lead to greater helplessness in the face of adversity, less self-responsibility and the idea that they do not have confidence in their own abilities to solve life problems
2. **Polypharmacy**: There is no support in the literature for combination therapy, and indeed there is consistency in that all the major guidelines recommend against this. Polypharmacy could indicate that treatment failures are not accepted as such
3. **Misuse/overdose**: clients may take the wrong dosage through an attempt at emotion regulation, or through misuse due to poor impulse managements, addiction problems or suicidal behaviour.
4. **Ineffective psychosocial treatment**: since medication is used to help manage emotions, thinking and behaviour, this may lead the client to lower their tolerance of emotions and motivation to work on psychological alternatives of learning new ways to manage emotions and impulses. They may learn that it is easier to seek an "escape" type strategy for their problems where they do not need to learn and practice new skills

Appendix 2: traffic light status of antipsychotic medicines for use in patients aged 18 or over

Oral antipsychotic medicines

<table>
<tr><th rowspan="2">Oral Antipsychotic</th><th rowspan="2">Generation</th><th colspan="4">Traffic light classification</th></tr>
<tr><th>Psychosis</th><th>Bipolar Affective Disorder</th><th>Adjunct in depression or psychotic depression</th><th>Non-cognitive symptoms of dementia</th></tr>
<tr><td>Chlorpromazine</td><td>1st Gen</td><td rowspan="3">Specialist initiation
Physical monitoring guideline applies (appendix 3)</td><td colspan="2" rowspan="3">Not usually prescribed for these indications.
If recommended 3rd line or subsequently, this must be initiated and the dose stabilised by a specialist.
The physical monitoring guideline applies (appendix 3)</td><td>DO NOT PRESCRIBE</td></tr>
<tr><td>Flupentixol</td><td>1st Gen</td><td rowspan="2">GREEN</td></tr>
<tr><td>Haloperidol</td><td>1st Gen</td></tr>
<tr><td>Promazine</td><td>1st Gen</td><td>DO NOT PRESCRIBE</td><td>DO NOT PRESCRIBE</td><td>GREY**</td><td rowspan="5">DO NOT PRESCRIBE</td></tr>
<tr><td>Sulpiride</td><td>1st Gen</td><td rowspan="4">Specialist initiation
Physical monitoring guideline applies (appendix 3)</td><td colspan="2" rowspan="2">Not usually prescribed for these indications.
If recommended 3rd line or subsequently, this must be by initiated and the dose stabilised by a specialist.
The physical monitoring guideline applies (appendix 3)</td></tr>
<tr><td>Trifluoperazine</td><td>1st Gen</td></tr>
<tr><td>Zuclopentixol</td><td>1st Gen</td></tr>
<tr><td>Amisulpride</td><td>2nd Gen</td><td>Specialist recommendation for chronic depressive symptoms, low dose only***</td></tr>
<tr><td>Aripiprazole</td><td>2nd Gen</td><td colspan="2">Specialist initiation
Physical monitoring guideline apples (appendix 3)</td><td>Specialist recommendation</td></tr>
<tr><td>Cariprazine*</td><td>2nd Gen</td><td>Red</td><td>DO NOT PRESCRIBE</td><td rowspan="2">DO NOT PRESCRIBE</td><td rowspan="2">DO NOT PRESCRIBE</td></tr>
<tr><td>Lurasidone</td><td>2nd Gen</td><td>Red</td><td>Red for BPAD depression</td></tr>
<tr><td>Olanzapine</td><td>2nd Gen</td><td rowspan="4">Specialist initiation
Physical monitoring guideline applies (appendix 3)</td><td colspan="2" rowspan="4">Specialist initiation
Physical monitoring guideline applies (appendix 3)</td><td rowspan="3">Specialist recommendation</td></tr>
<tr><td>Quetiapine</td><td>2nd Gen</td></tr>
<tr><td>Quetiapine MR</td><td>2nd Gen</td></tr>
<tr><td>Risperidone</td><td>2nd Gen</td><td>GREEN</td></tr>
<tr><td>Clozapine</td><td>2nd Gen</td><td>Red</td><td>Red</td><td></td><td></td></tr>
<tr><td>Paliperidone (oral)</td><td>2nd Gen</td><td colspan="4">DO NOT PRESCRIBE</td></tr>
<tr><td>Asenapine</td><td>2nd Gen</td><td colspan="4">DO NOT PRESCRIBE</td></tr>
</table>

(*) Women of childbearing potential must use highly effective contraception while taking cariprazine and at least for 10 weeks after stopping treatment. Women using systemically acting hormonal contraceptives should add a second (barrier) method.
(**) Licensed for short-term adjunctive management of psychomotor agitation and for agitation and restlessness in the elderly
(***) Recommended in NICE NG222 as an option for treatment of chronic depression at low doses (max 50mg/day): physical monitoring guideline does not apply in this context

Depot and long-acting injectable antipsychotic medicines

Depot/LAI Antipsychotic	Generation	Suggested classification
Flupentixol decanoate	1st Gen	Red
Haloperidol decanoate	1st Gen	
Zuclopenthixol decanoate	1st Gen	
Aripiprazole (Abilify Maintena®)	2nd Gen	
Paliperidone (Xeplion®)	2nd Gen	
Risperidone (Risperdal Consta®)	2nd Gen	
Olanzapine embonate[5]	2nd Gen	Red

[5] The SmPC for Olanzapine embonate requires that it is administered in a medical facility because of the risk of a post-injection syndrome

Appendix 3: Antipsychotics- Recommended Physical Monitoring in Severe Mental Illness

Health check results/outcomes to be shared between healthcare providers

Baseline monitoring - to be done by the initiating organisation

U&Es; FBC; LFTs; TFTs; prolactin; Fasting/random glucose/HbA1C; Lipids/CVD risk calculation BP & pulse; Weight/BMI; waist circumference; CKD screen; lifestyle (smoking (no/day), diet, physical activity)

ECG –where mandated for specific antipsychotics eg haloperidol, identified CV risk, family history, additive risk with concurrent medication

Monitoring in the first 6 weeks – to be done by the initiating organisation

Weekly weight. Rapid weight gain (5kg < 3 months) - review choice of antipsychotic

Monitoring at 3 months – to be done by the initiating organisation

Weight/BMI; BP & pulse; glucose/BbA1C
Lipid profile/CVD risk; lifestyle

Assessment at 12 months

If initiated in secondary care the psychiatrist will send a copy of this guideline and the person's care plan with latest blood results to the GP.

U&Es; FBC; LFTs; Fasting/random glucose/HbA1C; Lipids/CVD risk calculation
BP & pulse; Weight/BMI; waist circumference; lifestyle (smoking (no/day), diet, physical activity)

Annual monitoring in primary care for those not in contact with secondary care (discharged or solely under care of primary services) and those under secondary care for 12 months whose condition has stabilised

Annual monitoring in primary care

General physical and cardiometabolic health; national screening programmes; medicines reconciliation and monitoring

1. enquire about smoking, alcohol and drug use
2. enquire about diet and activity levels
3. check blood pressure & pulse
4. cv risk assessment
5. measurement of body mass index (BMI)
6. check for the development of diabetes
7. check renal function
8. follow up national screening where appropriate eg breast/cervical/bowel
9. sexual health screening, contraception etc
10. check the accuracy of the record of medication prescribed by the General Practitioner and the Psychiatrist
11. if new medicines or changes to physical health have increased the risk of prolonged QTc arrange ECG. prescribed by the General Practitioner and the Psychiatrist

Remember to ask about sexual side effects.
Check prolactin if symptomatic

Remember to ask about smoking habits. Cigarette smoke can alter the metabolism of medicines particularly clozapine.
Plan quit attempts with the psychiatrist

Collaborate with specialist services where:

- Poor response to treatment
- Non adherence to medication
- Intolerable side effects of medication
- Co-morbid substance misuse
- Physical health concerns indicate review required eg deteriorating CKD and dose prescribed

Physical health monitoring in people with serious mental illness prescribed antipsychotics

Background

Life expectancy in people with severe mental illness (SMI) is reduced by 15-20 years compared with the general population. Individuals with SMI have double the risk of obesity and diabetes, three times the risk of hypertension and metabolic syndrome and five times the risk of dyslipidaemia than the general population.

There is a concern that some antipsychotic drugs, particularly atypicals, have metabolic consequences that contribute to the risk. Atypical antipsychotics are known to cause weight gain and impact on the lipid profile. They may also have a direct effect on insulin function, independent of weight gain. Metabolic effects are also seen in patients prescribed typical antipsychotics.

DHCFT supports the use of the cardiometabolic health resource known as the LESTER framework for patients prescribed all antipsychotics. This is in line with the NHS England guidance for CCGs published in February 2018 'Improving physical health care for people living with severe mental illness in primary care'.

This policy is based on LESTER, the NHS England guidance for CCGs and with additional recommendations to guide safe care appropriate to antipsychotic use.

Monitoring

This policy outlines the minimum recommended standards and does not preclude the monitoring of additional parameters tailored to individual patients as clinically indicated. Patients may require more frequent monitoring e.g those patients with increased cardiac risk or existing diagnosis of diabetes.

QTc

Antipsychotics may prolong the QTc interval; normal QTc intervals are <450 milliseconds (ms) for men and <460 ms for women. A QTc between these values and 500 ms is considered prolonged. A prolonged QTc or one that is increasing over time should be monitored, see Identifying risk factors for developing a long QT interval

A QTc of >499mSec is a **RED FLAG** and should be acted upon. (1. Check the machine has worked it out correctly by doing the calculation yourself. 2. Review other QTC lengthening meds (www.crediblemeds.org) and get a K, Mg & Ca blood test and correct. 3. Consider reducing dose of antipsychotic immediately (and then thinking what to do next wrt effective meds) and repeat ECG in a week. 4. Consult cardiologist if in doubt.) [1]

Smoking

Cigarette smoke is a potent inducer of the liver enzyme known as cytochrome P450 1A2 (CYP1A2). Drug levels in the blood may be affected if a patient stops smoking tobacco and this effect will also apply if Nicotine Replacement therapy (NRT) is being used. Mental health practitioners will also need to consider the potential for fluctuation in effect when tobacco use is not consistent. Significant effects have been reported in patients who change smoking habits while prescribed Clozapine. Quit attempts should be planned in conjunction with the psychiatrist (SPS considering drug interactions with smoking).

Reference

- Advice from Dr Sandler, Cardiologist, CRH July 2012
- NHS England 'improving physical health care for people living with severe mental illness in primary care' guidance for CCGs February 2018
- LESTER positive cardiometabolic health resource