SHARED CARE GUIDELINE

Pennine Care NHS
NHS Foundation Trust

Title: Prescribing and Monitoring of Antipsychotics

Scope: Pennine Care NHS Foundation Trust NHS Bury NHS Oldham NHS Heywood, Middleton and Rochdale NHS Stockport NHS Tameside & Glossop	**Version:** Version 1

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To be read in conjunction with the following documents:	1. British National Formulary (BNF). Latest edition. http://bnf.org 2. Summary of Product Characteristics (SPC) for individual second generation antipsychotics http://www.medicines.org.uk/emc 3. NICE Clinical Guideline 82 Schizophrenia (March 2009) http://guidance.nice.org.uk/CG82/QuickRefGuide/pdf/English 4. Pennine Care clinical guidelines as referred to in the text. http://penninenet/intranet/department.asp?deptID=198
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1. Introduction

Antipsychotic drugs are used variously in the long-term treatment of schizophrenia and other psychoses, mania, depression (including bipolar depression) and in other chronic conditions according to their individual product licences. They may also be used in the short-term treatment of such conditions as anxiety, psychomotor agitation, and violent or dangerously impulsive behaviours, however such applications fall outside the scope of this guideline.

Antipsychotic drugs have been traditionally separated into two groups; typical and atypical, or first and second generation based upon their side-effect profiles. However,

> There is little meaningful difference in efficacy between each of the antipsychotic drugs (other than clozapine), and response and tolerability to each antipsychotic drug varies. There is no first-line antipsychotic drug which is suitable for all patients. Choice of antipsychotic medication is influenced by the patient's medication history, the degree of sedation required and consideration of individual patient factors….
> (BNF 62 September 2011).

NICE guideline 82 (Schizophrenia) recommends that choice of drug treatment should be made after an informed discussion between patient and prescriber. (See also Pennine Care MM039 Guidelines for the prescribing and monitoring of antipsychotics in the treatment of schizophrenia.)

This Shared Care Guideline covers the use of the full range of antipsychotic drugs in the prescribing and monitoring of long-term treatment procedures.

2. Scope

Pennine Care NHS Foundation Trust
NHS Bury
NHS Heywood, Middleton and Rochdale
NHS Oldham
NHS Stockport
NHS Tameside & Glossop

3. Clinical Conditions being treated

See Table 1

TABLE 1 - Summary of Licensed Indications, Formulations and Dosage

Full information may be found in the BNF or individual SPCs.

DRUG	INDICATION(S)	DOSAGE RANGE	FORMULATION
amisulpride (generic)	schizophrenia	predominately negative symptoms - 50-300mg daily in two divided doses acute psychotic episode 400mg –800mg daily in divided doses max 1.2g daily	tablets 50mg, 100mg, 200mg, 400mg solution 100mg/ml
aripiprazole (Abilify)	schizophrenia mania	10mg – 30mg daily *Enhanced efficacy at doses higher than a daily dose of 15mg has not been demonstrated although individual patients may benefit from a higher dose.*	tablets 5mg, 10mg, 15mg, 30mg orodispersible tablets 10mg, 15mg solution 1mg/ml
chlorpromazine (generic)	schizophrenia/ psychosis, mania	75mg daily, in three divided doses, adjusted to range 75-300mg daily max 1g	tablets 25mg, 50mg, 100mg solution25mg/5ml
clozapine (Clozaril, Denzapine) *Normally prescribed and monitored in secondary care only.*	treatment resistant schizophrenia	200-450mg daily in two divided doses (max 900mg)	tablets 25mg, 100mg
	psychosis in Parkinson's disease	25-37.5mg bedtime max 100mg daily	
flupentixol (Depixol)	schizophrenia/ psychosis	3-9mg twice daily max 18mg daily	tablets 3mg
		20-40mg every 2-4 weeks max 400mg weekly	long-acting intramuscular(IM) injection 20mg/ml, 100/ml, 200mg/ml

fluphenazine decanoate (Modecate)	schizophrenia/ psychosis	12.5-100mg repeated at intervals of 14-35 days	long-acting IM injection 25mg/ml; 0.5ml, 1ml, 2ml ampoules 100mg/ml; 0.5ml, 1ml ampoule
haloperidol decanoate (generic)	schizophrenia/ psychosis, mania	0.5-3mg two to three times daily, adjusted to range 3-5mg, two to three times daily max 30mg	tablets 0.5mg, 1.5mg, 5mg, 10mg, 20mg liquid 1mg/ml, 2mg/ml
	schizophrenia/ psychosis	50mg every 4 weeks adjusted to max 300mg every 4 weeks	long-acting IM injection 50mg/ml, 100mg/ml
paliperidone (Xepilon)	schizophrenia	150mg on day 1, 100mg on day 8, then every 4 weeks in the range 25-150mg	long-acting IM injection
olanzapine (generic)	schizophrenia; combination therapy for mania; preventing recurrence in bipolar disorder	5-20mg daily (max 20mg)	tablets 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg orodispersible tablets 5mg, 10mg, 15mg, 20mg
	mania (monotherapy)	15mg daily	
perphenazine (Fentazin)	schizophrenia/ psychosis, mania	4mg three times a day adjusted according to response max 24mg	tablets 2mg, 4mg
pipotiazine palmitate (Piportil Depot)	schizophrenia/ psychosis	50-100mg every 4 weeks max 200mg	long-acting IM injection 50mg/ml; 1ml, 2ml ampoules

quetiapine (generic)	schizophrenia	300-450mg daily in two divided doses *(after 5 day dose titration)* max 750mg daily	tablets 25mg, 100mg, 150mg, 200mg, 300mg
	mania; treatment/prevention	400 – 800mg daily in two divided doses *(after 5 day dose titration)*	
	depression in bipolar disorder	300mg at bedtime *(after 5 day dose titration)* max 600mg	
quetiapine MR (Seroquel XL)	schizophrenia	600mg daily *after 2 day dose titration* max 800mg	modified release tablets 50mg, 150mg, 200mg, 300mg, 400mg
	mania; treatment/prevention	400-800mg daily *after 2 day dose titration*	
	depression in bipolar disorder	300mg daily *after 3 day dose titration* max 600mg	
	major depression: adjunctive treatment	150-300mg daily *after 2 day dose titration*	
risperidone (generic)	psychosis	4-6mg daily in two divided doses *after 2 day dose titration* *doses above 10mg only if benefit outweighs risk* max 16mg	tablets 0.5mg, 1mg, 2mg, 3mg, 4mg, 6mg orodispersible tablets 0.5mg, 1mg, 2mg,3mg,4mg liquid 1mg/ml
	mania	2mg daily, increased by steps of 1mg daily; dose range 1-6mg	

risperidone (Risperidal Consta)	schizophrenia/ psychosis	25mg every two weeks, adjusted according to response to max 50mg every two weeks	long-acting IM injection 25mg, 37.5mg, 50mg vials
sulpiride (generic)	schizophrenia	200-400mg twice daily max 800mg in mainly negative symptoms max 2.4mg daily in mainly positive symptoms	tablets 200mg, 400mg solution 200mg/5ml
trifluoperazine (generic)	schizophrenia/ psychosis	5mg twice daily, adjusted according to response	tablets 1mg, 5mg syrup, 1mg/5ml
zuclopenthixol (Clopixol)	schizophrenia/ psychosis	20-50mg daily in divided doses according to response max 150mg	tablets 2mg, 10mg, 25mg
zuclopenthixol decanoate **NB not to be confused with zuclopenthixol acetate injection** -for specialist use in in-patient services only		200-500mg every 1-4 weeks adjusted according to response max 600mg weekly	long-acting IM injection 200mg/ml, 500mg/ml

4. Product information and treatment regimens to be used

Treatment with antipsychotics will most usually be initiated within secondary care.

Specialist mental health services will provide information on choice of drug, route of administration, initiation, titration and dosage.

Newly-diagnosed patients are normally offered **oral medication**, in the form of tablets or capsules. However, if there are swallowing difficulties, **oro-dispersible** tablets, which dissolve rapidly in the saliva, may be considered. These may also be taken after dispersal in water or fruit juice. Long acting intramuscular **antipsychotic injections** ('depots') may be considered where compliance with oral medication is a barrier to recovery. In some boroughs, treatment with depots is prescribed by the general practitioner (GP); in others it is provided via the boroughs' depot clinics.
(Please refer to MM014 Guidelines for the administration of antipsychotic depot injections)

The use of **risperidone, olanzapine and paliperidone** long acting injections is restricted in Pennine Care. (Please refer to MM033, MM059 and MM071 for the appropriate guidelines).

The BNF recommends that the balance of risks and benefits should be considered before prescribing antipsychotic drugs to those **over the age of 65**. It is recommended that:

- Antipsychotic drugs should be used with caution in elderly patients
- Initial doses should be at half the adult dose or less, taking into account the patient's weight, co-morbidity and concomitant medication.
- Treatment should be reviewed regularly

There is little information on the efficacy and safety of antipsychotic drugs in **children and adolescents**; in particular little is known about their long term effects on the developing nervous system. Antipsychotic drugs should therefore be initiated and managed under the close supervision of an appropriate specialist.

Monitoring clinical outcomes and side effects will generally take place within specialist mental health services.

Monitoring of physical healthcare will generally take place in primary care.

5. Regimen Management

Consultant/Specialist mental health services will

a) perform mental health assessment prior to starting antipsychotics.

b) discuss with the patient and carer the benefits and side-effects of different antipsychotic drugs, and agree on a mutually acceptable treatment regime.

c) initiate antipsychotic treatment, including titration of dosage until a stable mental state is achieved, where required.

Alternatively, by agreement, provide information to the GP to enable prescribing to be initiated in primary care.

d) perform or recommend baseline tests before treatment is commenced. These should include:

- weight
- fasting blood glucose
- blood pressure and pulse
- blood lipids
- urea and electrolytes
- full blood count
- liver function
- electro cardiogram (ECG) where clinically indicated, or if haloperidol is to be prescribed.
- prolactin

Baseline tests may be carried out in primary care but this needs to be agreed with the GP in advance.

e) agree with GP to share care after initiation.

f) inform the GP of patients' response to medication, mental state and general progress at appropriate intervals.

g) monitor for side-effects (see BNF section 4.2.1 Side-effects) and take appropriate action.

h) inform the GP of any change in medication, or dosage regime.

j) advise the GP about the discontinuation of treatment, where required, and provide advice about necessary supervision afterwards.

k) report suspected adverse drug reactions via the Yellow Card Scheme www.mhra.gov.uk/yellowcard

GP / Primary Care Services

a) reply to the request for shared care as soon as is possible.

b) provide regular prescriptions for antipsychotics as per guidance from specialist services/ secondary care.
- This does not normally include clozapine, which is usually supplied by hospital prescription.
- In some boroughs GPs are asked to prescribe long-acting and depot

antipsychotic injections. In others, these are provided in the community mental health teams' (CMHT) depot clinics.

c) provide appropriate physical health monitoring (see BNF section 4.2.1.Monitoring, and Appendix 1)
   - send copies of all laboratory results to the consultant/specialist team
   - refer patient to appropriate medical specialist as necessary

d) liaise with the consultant/ specialist services regarding concerns about any changes to the patients' mental state, and refer to the consultant in cases of significant clinical deterioration.

e) follow specialist advice regarding changes to the medication, or dosage, or route of administration.

f) discontinue of treatment if required on the advice of the consultant/ specialist service.

g) report suspected adverse drug reactions via the Yellow Card Scheme www.mhra.gov.uk/yellowcard

6. Special Considerations

Patients should be informed that there is a high risk of relapse if medication is not taken as directed, and/or if medication is stopped within 1-2 years. Patients should be encouraged to discuss problems with side effects or compliance, and appropriate changes should be put in place. A change of drug, dosage or formulation may need to be made.

Withdrawal of antipsychotic drugs after long-term therapy should always be gradual and closely monitored to avoid the risk of acute withdrawal symptoms or rapid relapse. Patients should be monitored for 2 years after withdrawal of antipsychotic medication for signs and symptoms of relapse.

7. Summary of cautions, contra indications, side effects

See BNF section 4.2.1 for cautions, contraindications, use in hepatic or renal impairment, and in pregnancy and breast-feeding.

8. Back-up care available to GP from Hospital, including emergency contact procedures and help line numbers.

The on-call psychiatric service covering the local hospital can be contacted via the switchboard of Pennine Care NHS Foundation Trust (0161 716 3000).

Where the concern relates to a specific known patient, and arises within office hours (9am - 5pm), then the sector consultant psychiatrist and GP should normally liaise with each other directly.

9. Statement of Agreement between GP and Consultant.

This is a request by the Consultant to share the suggested care pathway of your patient. If the GP is unable to agree to the sharing of care and/or of initiating the suggested medication, please make this known to the Consultant within 14 days, ideally stating nature of his/her concern.

10. Written information provided to patient

Leaflet provided by specialist services if available, otherwise manufacturer's Patient Information Leaflets (provided by pharmacy).

APPENDIX 1 - MONITORING

Adapted from The Maudsley Prescribing Guidelines. 10th edition, 2009
(See also BNF, section 4.2.1 Monitoring, and Pennine Care MM063 Guidelines for the management of patients who have antipsychotic induced weight gain)

Parameter/test	Suggested frequency	Action to be taken if results outside reference range	Drugs with special precautions	Drugs for which monitoring is not required
Urea and electrolytes (including creatinine or estimated GFR)	Baseline and yearly	Investigate all abnormalities detected	Amisulpride renally excreted – consider reducing dose if GFR reduced	None
Full blood count (FBC)	Baseline and yearly	Stop suspect drug if neutrophils fall below 1.5 x 10^9/1. Refer to specialist medical care if neutrophils below 0.5 x 10^9/1. Note high frequency of benign ethnic neutropenia in certain ethnic groups	Clozapine – FBC weekly for 18 weeks, then fortnightly upto 1 year, then monthly	None
Blood lipids (cholesterol; triglycerides) Fasting sample, if possible	Baseline, at 3 months, then yearly	Offer lifestyle advice. Consider changing antipsychotic and/or statin therapy	Clozapine, olanzapine, quetiapine, phenothiazines – 3 monthly for first year, then yearly	Some not clearly associated with dyslipidaemia but prevalence is high in this patient group
Weight (include waist size and BMI, if possible)	Baseline, frequently for 3 months, then yearly	Offer lifestyle advice. Consider changing antipsychotic and/or dietary/pharmacological intervention	Clozapine, olanzapine – frequently for 3 months then 3 monthly for first year, then yearly	Aripiprazole not clearly associated with weight gain but monitoring recommended nonetheless – obesity prevalence high in this patient group

Plasma glucose (fasting sample, if possible)	Baseline, at 4-6 months, then yearly	Offer lifestyle advice. Obtain fasting sample and HbA_{1C}. Refer to GP or specialist	Clozapine, olanzapine – test at baseline, 1 month, then 4-6 monthly	Some not clearly associated with IFG but prevalence is high in this patient group
ECG (recommended for all inpatients as per NICE guidance)	Baseline, where clinically indicated and after dose increases	Refer for further investigations if appropriate	haloperidol – ECG mandatory	
Blood pressure	Baseline; frequently during dose titration	If severe hypotension or hypertension (clozapine) observed, slow rate of titration	Clozapine, chlorpromazine and quetiapine most likely to be associated with postural hypotension	Amisulpride, aripiprazole, trifluoperazine, sulpiride
Prolactin	Baseline, then at 6 months, then yearly	Switch drugs if hyperprolactinaemia confirmed and symptomatic		Aripiprazole, clozapine, quetiapine, olanzapine (<20 mg), but worth monitoring if symptoms arise
Liver function tests (LFTs)	Baseline, then yearly	Stop suspect drug if LFTs indicate hepatitis (transaminases x 3 normal) or functional damage (PT/albumin change)	Clozapine associated with hepatic failure	Amisulpride, sulpiride

Other tests:
Patients on clozapine may benefit from an **EEG** as this may help determine the need for valproate. Those on quetiapine should have **thyroid** function tests yearly, although the risk of abnormality is very small.

Key:
BMI, body mass index; ECG, electrocardiograph; EEG, electroencephalogram; GFR, glomerular filtration rate; IFG, impaired fasting glucose