Mental Health Service

MHS 34 - High Dose Antipsychotic Monitoring Policy

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Important Note:
The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

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Revision/Amendment Information

Please record brief details of the changes made alongside the next version number. If the procedural document has been reviewed **without change**, this information will still need to be recorded although the version number will remain the same.

Version	Date	Brief Summary of Changes	Author(s)
1.0	July 2012	First approved version	PMG (MH)
2.0	July 2015	Reviewed	PMG (MH)
3.0	July 2018	Name changed to 'high dose antipsychotic monitoring policy' from 'high dose antipsychotic therapy guideline' Page 4 Recent GG&C audit results added Page 5 Policy key points reviewed and updated Page 6 Risk factors and drug interactions updated and tabulated Page 7 Monitoring requirements updated and tabulated Page 7,8 Threshold for prolonged QTc interval updated in line with GG&C guidance Page 8 Addition of problems associated with high dose antipsychotic therapy including clarification of normal, borderline and prolonged QTc interval Page 9 Off-label/ liability issues added Page 9 Roles and responsibilities updated to reflect new policy statements Page 10 Review of antipsychotics and doses Page 10 Haloperidol and QTc contraindication added Page 11 Review and update of audit criteria to reflect new policy statements. Removal of audit tool Page 11 References updated Page 12 Review and update of high dose monitoring form Removal of 'Prescribing Guidance: The Use of more than one antipsychotic drug at the same time' Removal of POMH ready reckoner	PMG (MH) SLWG
4.0	August 2025	Appendix 3- Monitoring form- Removed as EMIS template available.	PMG (MH)

Contents

This guideline was reviewed by the Prescribing Management Group (Mental Health)

1. Introduction and Background

The Consensus statement on high-dose antipsychotic medication (Royal College of Psychiatry Council Report CR190, November 2014)[1] defines high-dose antipsychotic use as:

A total daily dose of a single antipsychotic which exceeds the upper limit stated in the summary of product characteristics (SPC) or BNF with respect to the age of the patient and the indication being treated.

or

A total daily dose of two or more antipsychotics which exceeds the summary of product characteristics (SPC) or BNF maximum using the percentage method.

High dose antipsychotic use should be the exception rather than the rule. Overall, the evidence from randomised controlled trials (RCTs) to support the use of combined antipsychotics in schizophrenia remains scarce. There is little convincing evidence that antipsychotics higher than the maximum licensed dose are more effective than standard dosage for treatment-resistant schizophrenia. In addition, the evidence for combining non-clozapine antipsychotics is generally weak.

Audit work within NHS GG&C MHS demonstrated that the use of a single antipsychotic at doses above the BNF maximum was relatively uncommon (<10%) with high dose antipsychotic use being much more likely with the use of combined antipsychotics (>90%). The majority of high dose combinations included the use of a long-acting injection antipsychotic and an oral antipsychotic (40%) with around 25% of high dose use resulting from augmentation of clozapine with a second oral antipsychotic. Audits will be carried out on an annual basis.

Prescribing of as required antipsychotics for acute behavioural disturbance may inadvertently contribute to high-dose antipsychotic use.

2. Scope

This policy applies to all staff working within NHS Greater Glasgow & Clyde Mental Health Services. This includes Adult, Older Adult, Learning Disability, Addiction, Forensic and Child & Adolescent Mental Health Services.

3. High dose antipsychotic monitoring policy

1. The responsibility to exceed the licensed dose of a single antipsychotic or to use a combination of more than one lies with the consultant psychiatrist responsible for the patient's care.

2. The decision to prescribe high dose antipsychotic therapy should be discussed with the multidisciplinary team (including a clinical pharmacist). If this is not possible, consider obtaining an informal second opinion from a local psychiatrist to support the use of high dose antipsychotic therapy.

3. The details of the clinical rationale for prescribing high dose antipsychotic therapy should be clearly documented within the patient's clinical notes.

4. The decision to prescribe high dose antipsychotic therapy and the rationale should be discussed with the patient and/or carer and valid consent obtained and documented. General advice about the unlicensed uses of licensed medications and QTc prolongation with antipsychotics is available from the Choice and Medication website[2] and may be useful in aiding discussions regarding high dose antipsychotic therapy. Unlicensed use handy fact sheet & QTc handy fact sheet

5. For patients receiving treatment under the terms of Mental Health (Care & Treatment)

(Scotland) Act 2003 or Adults with Incapacity (Scotland) Act 2000, ensure that the statutory treatment plan on a T2B or T3B certificate or section 47 includes the use of doses in excess of BNF guidelines or combinations of antipsychotics and reference the recommended monitoring within this policy prior to prescribing.

6. CMHTs and wards should maintain a local register of patients prescribed high dose antipsychotic therapy to ensure that the recommended monitoring is undertaken. All patients must have a warning added to their EMIS record

7. High dose antipsychotic therapy may be prescribed in an emergency for acute symptoms. This should be discussed with a senior psychiatrist before it is prescribed.

8. The following issues should be considered at baseline and ongoing as per monitoring recommendations and documented on the high dose monitoring template on EMIS:

    - Rationale for treatment
    - Consent or compliance with statutory treatment plans
    - Details of antipsychotics (drug names and doses) prescribed
    - Risk factors
    - Drug interactions
    - Monitoring completed and any actions as a result of abnormalities
    - Symptom rating scales
    - Side effect rating scales
    - When monitoring is next due

9. If a patient refuses to consent to high dose antipsychotic monitoring, then this should be clearly documented within their clinical notes. Ongoing refusal to engage with monitoring must prompt review and consideration of cessation of high dose antipsychotic therapy.

10. High dose antipsychotic therapy should be reduced to conventional dosing if no significant improvement is observed at review.

11. Communication at transition. Ensuring good communication at points of transition (e.g. between inpatient care and CMHT) with regards to the rationale for high dose antipsychotic therapy, results of monitoring completed and when monitoring is next due is vital to ensure optimum patient care.

4. Risk Factors and Drug Interactions

Risk factors and potential drug interactions must be considered prior to prescribing high dose antipsychotic therapy and at each review.

Risk factor	Rationale for potential risk of QT prolongation
Cardiac history	▪ particularly myocardial infarction, arrhythmias, bradycardia, abnormal ECG, long QT syndrome, heart failure ▪ consider family history
Hepatic impairment	▪ potential impact on hepatic metabolism and clearance of antipsychotics ▪ QT prolongation is increased in alcoholic liver disease
Renal impairment	▪ potentially decreases clearance of renally excreted antipsychotics ▪ may increase risk of electrolyte disturbance
Alcoholism	▪ increased risk of hepatic impairment
Smoking	▪ increased risk of ischaemic heart disease ▪ impact on hepatic metabolism of some antipsychotics
Substance misuse	▪ due to risk of QT prolongation with certain substances
Old age	▪ elderly more susceptible to QT changes
Extremes of weight	▪ impact of obesity on CV risk and hepatic function ▪ very low BMI increases risk of electrolyte abnormalities and dehydration
Female gender	▪ women have longer QT intervals
Extreme physical exertion	▪ e.g. individuals subject to restraint

Drug interactions	Rationale for potential risk of QT prolongation
Medications known to prolong QT interval including anti-arrhythmics*	▪ a list of medications known to prolong the QT interval can be found at https://www.crediblemeds.org[3] (an American website which categorises medications based on their risk)
Pharmacokinetic interactions	▪ medications that increase antipsychotic plasma levels. (NB smoking can decrease plasma levels of some antipsychotics, especially clozapine, therefore, smoking cessation will increase plasma levels and may require dose reduction)
Medications known to cause electrolyte disturbance e.g. diuretics	▪ electrolyte abnormalities e.g. hypokalaemia, hypocalcaemia, hypomagnesaemia can increase the risk of QT prolongation

*Promethazine, which is commonly used as an anxiolytic, hypnotic and in the management of acutely disturbed behavior, may have an additive effect when administered alongside other drugs that prolong QTc and caution is advised with patients at higher risk.

5. Monitoring

At initiation of high dose antipsychotic therapy, a plan for ongoing monitoring must be agreed for the individual patient including;

- frequency of monitoring *
- responsibilities for monitoring and checking results
- regular review of progress.

* It is recommended that increased monitoring is undertaken when using higher risk therapy e.g. haloperidol, diuretics, concurrent medications known to cause QT prolongation or those with other risk factors.

High Dose Antipsychotic Monitoring & Frequency*		
Monitoring	**Baseline**	**Ongoing**
ECG	Yes If a prolonged QT interval is recorded at baseline (QTc > 450msec in men and > 460msec in women), review treatment. Consider cardiology assessment. If it is decided to continue treatment, record reasons for doing so in patient's case notes.	• When steady state serum levels have been reached after each dose increment (consult a clinical pharmacist for advice on appropriate timescales) • Then every 6-12 months *
U&Es	Yes	• Every 6 months *
LFTs	Yes	• Every 6 months *
Lipids Blood glucose and/or HbA1c (for high dose therapies with increased risk of metabolic disturbance)	Yes	• Every 6 months *
Standard observations (bp, pulse, temperature)	Yes	• At least every 6 months* • Following dose escalation, monitor for any deterioration in physical health.
Review of progress and ongoing need for HDAT		• Every 3 months
Symptom rating scales e.g. CGI	Yes	• At 6 weeks • At 3 months • Then at least annually *
Side rating scales e.g. GASS or LUNSERS	Yes	• At 6 weeks • At 3 months • Then at least annually *

With the exception of clozapine, plasma level monitoring is not routinely carried out for antipsychotics. In patients exhibiting signs of adverse effects/toxicity or where other risk factors are present, plasma level monitor of antipsychotics could be considered where assays and reference ranges are available.

6. Management of Problems Associated With High Dose Antipsychotic Therapy

Management of QTc prolongation in high dose antipsychotic therapy [4]			
QTc Interval*	**Males**	**Females**	**Recommendations**
Normal	<460ms	<470ms	No action unless abnormal T-wave morphology [5]
Borderline prolonged	>450 ms but <500ms	>460ms but <500ms	Consider dose reduction and/or switching to a drug of lower effect on QTc Repeat ECG
Prolonged	>500ms	>500ms	Immediate review and cessation of high dose therapy Switch to drug of lower effect on QTc Repeat ECG
A change in baseline QTc of >20ms should raise concern and should be assessed in conjunction with the overall QTc interval.			

*The QT interval is lengthened at slower heart rates and shortened at faster heart rates and therefore needs adjusted for heart rate, producing the widely used QTc (the corrected QT interval).
There are several calculations available to correct the QT interval, with Bazett being the most widely used formula and the one used by many ECG machines to calculate automated QTc[4]. GGC medicines update- Interpretation of the QTc Interval and Drug- Induced QTc Prolongation

Management of electrolyte disturbance in high dose antipsychotic therapy		
Electrolyte disturbance	**Reference range**	**Actions**
Hypokalaemia	K < 3.5mmol/l	Low K and Mg in particular can increase the risk of QTc prolongation. Consider the risk of electrolyte disturbance in the event of diarrhoea/vomiting or if diuretic therapy commenced. Address electrolyte disturbance, repeat U&Es and ECG
Hypomagnesaemia	Mg < 0.7mmol/l	
Hypocalcaemia	Adjusted Ca < 2.1mmol/l	

Management of adverse effects in high dose antipsychotic therapy (Weigh up any perceived benefits of high dose treatment vs adverse effects)	
Adverse effects	**Action**
Extrapyramidal side effects (EPSE)	Consider decreasing antipsychotics to conventional dosing
Metabolic side effects	Where high dose treatment or combination is associated with an increased risk of metabolic adverse effects, consider a change to treatment or manage metabolic changes appropriately

7. Off Label Use of Medication And Liability

Off-label medication use refers to the use of a licensed medicine outside the terms of its Marketing Authorisation (MA) (or product license). The use of a single antipsychotic used in excess of doses recommended within the BNF or SPC would constitute off-label prescribing.[1] In addition, using two medications concurrently where the combined use is contraindicated would also constitute off-label prescribing e.g. the combined use of haloperidol with another antipsychotic.

Prescribing of a licensed medicine outside the recommendations of the MA alters the prescriber's professional liablility.[1,6] The prescriber is always responsible for the use of medicines and in the event of adverse reactions associated with prescribed medication may be called upon to justify the decisions they have made.[7]

8. Roles and Responsibilities

It is essential to ensure clear lines of roles and responsibilities in relation to high dose antipsychotic monitoring are agreed within the team prior to commencing high dose antipsychotic therapy. Responsibilities may vary depending on the location of the patient and the multidisciplinary team members involved in their care.

Medical staff responsibilities:

- Discuss with multidisciplinary team and/or obtain informal second opinion prior to prescribing high dose antipsychotic therapy
- Document rationale for high dose antipsychotic therapy within clinical notes
- Discuss rationale with patient and/or carer and document consent
- Ensure statutory treatment plan on a T2B or T3B certificate or section 47 includes the use of doses in excess of BNF guidelines and reference the recommended monitoring within this policy prior to prescribing (where patient is subject to compulsory treatment)
- Develop and agree an individualised monitoring plan (dependent on risk factors, drug interactions and antipsychotic(s) prescribed)
- Ensure a system by which the required monitoring is completed, and any abnormal results are acted upon where appropriate
- Ensure at transition of care that other nursing/medical colleagues with a responsibility for prescribing and/or monitoring are informed of the patient's high dose antipsychotic therapy
- **High dose antipsychotic initiation is the responsibility of the consultant psychiatrist**

Key worker responsibilities:

- Ensure that high dose antipsychotic therapy is discussed at review
- Ensure high dose antipsychotic monitoring is highlighted within nursing care plan
- Undertake standard observations as per monitoring plan for patient
- Complete side effect rating scales with patient or ask patient to complete self-assessment side effect rating scales as per monitoring plan

Nurse team leader/ Senior charge nurse responsibilities:

- Ensure that ward/ CMHT has a current register of all patients treated with high dose antipsychotic therapy
- Ensure that regular review and monitoring is undertaken for all patients on high dose antipsychotic register

Pharmacist responsibilities (for inpatients):

- Discuss treatment options/ alternatives with medical staff
- Highlight high dose antipsychotic therapy on HEPMA and EMIS record
- Record initial high dose antipsychotic monitoring on EMIS at multidisciplinary review
- Support patient education

Non-medical prescribers can alter the dose of antipsychotic(s) in line with a treatment plan agreed by the multidisciplinary team.

Appendix I:

Maximum doses of antipsychotics and identification of patients on high dose antipsychotic therapy

In defining what constitutes high dose antipsychotic therapy for patients receiving more than one antipsychotic, use the percentage method for calculating high dose status. When expressed as a percentage of their respective recommended maximum dose and added together, a cumulative dose of greater than 100% is considered 'high dose'.

For example: clozapine 700mg and amisulpride 400mg daily.
Sum %= 78% + 33% = 111% (>100%, therefore high dose)

Antipsychotic	Maximum licensed adult dose (mg/day) 100% BNF maximum
Amisulpride	1200
Asenapine***	20
Aripiprazole oral/IM	30
Cariprazine	6
Chlorpromazine	1000
Clozapine	900
Flupentixol	18
Haloperidol oral/ IM *	20
Lurasidone	148
Olanzapine oral/IM	20
Paliperidone***	12
Pericyazine	300
Perphenazine	24
Pimozide**	20
Prochlorperazine	100
Promazine	800
Quetiapine	750 (Mania 800)
Risperidone	16
Sulpiride	2400
Trifluoperazine	50 (suggested by POMH****)
Zuclopenthixol	150

Depots/ Long-acting injections	Maximum licensed adult dose (mg/ time interval) 100% BNF maximum
Aripiprazole LAI	400 /month
Flupentixol decanoate	400 /week
Haloperidol decanoate	75 /week
Olanzapine embonate***	300 /fortnight
Paliperidone LAI (Xepilon)	150 /month
Paliperidone 3/12 LAI (Trevicta)***	525 /3 months
Paliperidone 6/12 LAI (Byannli)***	1000 /6 months
Risperidone LAI (Consta)	50 /fortnight
Zuclopenthixol decanoate	600 /week

Use of 'as required' (or 'prn') antipsychotic medication should also be taken into account.

* The use of haloperidol is contraindicated in combination with drugs that prolong the QTc interval and therefore, where possible the use of haloperidol in combination with other antipsychotics should be avoided. Haloperidol and QTc interval prolongation April 2023
** Subject to annual ECG irrespective of dosage.
*** Non formulary preparations within NHS GG&C MHS
**** Prescribing Observatory for Mental Health. POMH. Ready reckoner version 11. January 24

Appendix II: High Dose Antipsychotic Monitoring Audit Criteria

	Criteria	Standard	Exception
1	All inpatients prescribed high dose antipsychotic therapy should have the an appropriate flag added to prescription record and EMIS	100%	None
2	Each ward/ CMHT has a register of all patients subject to high dose antipsychotic monitoring	100%	None
3	There is evidence of documentation of rationale for high dose antipsychotic therapy	100%	None
4	There is documented evidence that consent from patient/ carer to prescribe high dose antipsychotic therapy was obtained	100%	Unless subject to compulsory treatment
5	T2B/ T3B certificate or section 47 make reference to high dose antipsychotic therapy and associated monitoring	100%	For those subject to compulsory treatments
6	The EMIS high dose monitoring template is in use for each patient	100%	None
7	The EMIS high dose monitoring template is completed correctly and is up to date	100%	None
8	There is evidence in the EMIS template of regular review of high dose antipsychotic therapy	100%	None

9. References:

1. Royal College of Psychiatrist College Report. Consensus statement on high-dose antipsychotic medication. CR 190. November 2014
2. Choice and Medication. Available at http://www.choiceandmedication.org/nhs24/
3. AZERT, Inc (2014) QTDrugs Lists. Available at https://www.crediblemeds.org/
4. GGC medicines update- Interpretation of the QTc Interval and Drug- Induced QTc Prolongation/ Published August 2023.
5. Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry. Wiley Blackwell. 14th edition
6. Baldwin DS, & Kosky N. Off-label prescribing in psychiatric practice. Adv Psych Treat 2007; 13:414–422
7. NHS GG&C Unlicensed Medicines Policy. October 2024.
8. Prescribing Observatory for Mental Health. POMH. Ready reckoner version 11. January 2024