GUIDELINES FOR THE USE OF HIGH DOSE ANTIPSYCHOTIC MEDICATION
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## 1. DOCUMENT CONTROL SUMMARY

<table>
<thead>
<tr>
<th>Document Title</th>
<th>Guidelines for the use of high dose antipsychotic medication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Document Purpose (executive brief)</strong></td>
<td>To provide guidance on the recognition of high dose antipsychotic regimes and the management of patients prescribed high dose antipsychotics</td>
</tr>
<tr>
<td><strong>Status: - New / Update/ Review</strong></td>
<td>Review</td>
</tr>
<tr>
<td><strong>Areas affected by the policy</strong></td>
<td>Patients prescribed antipsychotics for serious mental illness</td>
</tr>
<tr>
<td><strong>Policy originators/authors</strong></td>
<td>Chief Pharmacist</td>
</tr>
<tr>
<td><strong>Consultation and Communication with Stakeholders including public and patient group involvement</strong></td>
<td>Medicines Management Committee 17/05/16 Clinical Directors and Lead Clinicians-General adult</td>
</tr>
<tr>
<td><strong>Archiving Arrangements and register of documents</strong></td>
<td>The Risk Management Team is responsible for the archiving of this guideline and will hold archived copies on a central register</td>
</tr>
<tr>
<td><strong>Equality Analysis</strong> (including Mental Capacity Act 2007)</td>
<td>MMP001 Control of Medicines Policy</td>
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<tr>
<td><strong>Training Needs Analysis</strong></td>
<td>See section 7</td>
</tr>
<tr>
<td><strong>Monitoring Compliance and Effectiveness</strong></td>
<td>See section 8</td>
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<tr>
<td><strong>Meets national criteria with regard to</strong></td>
<td></td>
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<td>NSF</td>
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<td>CQC</td>
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<tr>
<td>Other</td>
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<tr>
<td><strong>Further comments to be considered at the time of ratification for this policy</strong> (i.e. national policy, commissioning requirements, legislation)</td>
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<tr>
<td><strong>If this policy requires Trust Board ratification please provide specific details of requirements</strong></td>
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2. INTRODUCTION

Majority of antipsychotic adverse effects are dose related and review of dose-response effects of a variety of antipsychotic have revealed little evidence for increasing doses above accepted licensed ranges. Combined antipsychotics have also been associated with longer hospital stay and more frequent adverse effects.

The use of high dose antipsychotics should be an exceptional clinical practice and the decision to use high doses should not be made lightly by a senior psychiatrist.

A high dose antipsychotic regime can result from either use of a single agent above the BNF limit or from a combination of two or more antipsychotics where each is within the maximum dose, however when each is expressed as a percentage of their BNF maximum and then added together, exceeds 100%.

Standard for Minimum Level of Physical Examination (CLP049) defines the level of physical health standard required for patient according to their lifestyle, medication and co-morbid conditions. The Trust Physical Healthcare Policy CLP070, highlighted that all healthcare staff are bound by the duty of care to ensure that the minimum level of physical health care of all patients within the care of Northamptonshire Healthcare NHS Foundation Trust (NHFT) is delivered, whether community, in-patient or outpatients.

3. PURPOSE

To provide guidance on the recognition of high dose antipsychotic regimes and the associated monitoring requirements for all patients prescribed high dose antipsychotics for serious mental health in the in-patient and outpatient NHFT services

4. DEFINITIONS

- ECG – Electrocardiogram
- U&E’s – Urea and electrolytes (used to monitor renal function)
- LFT’s Liver function tests (used to monitor liver function)
- GP- General Practitioner
- NHFT - Northamptonshire Healthcare NHS Foundation Trust

High Dose Antipsychotic - Single antipsychotic drug prescribed at a daily dose above the BNF upper recommended limit (High-dose single drug) or more than one antipsychotic prescribed concurrently (High-dose through the prescribing of multiple drugs)

See Appendix 1 for identification of patients on high dose antipsychotic medication
5. DUTIES

5.1. Medicines Management Committee
- Will approve and review these guidelines, and commission regular audit of treatment to check that the guidelines are being used appropriately

5.2. Medical Director
- Is responsible for the dissemination of this guideline to their Clinical Director’s and Clinical Tutor’s

5.3. Clinical Director’s
- Responsible for the dissemination and implementation of the guideline in their service areas
- Facilitating systems that will ensure patients prescribed high dose or combination antipsychotics are appropriately monitored, at least annually

5.4. Responsible Clinicians/ Consultants Psychiatrists
- Hold the sole responsibility to prescribe high dose antipsychotic or a combination of more than one antipsychotic over a specified trial period
- Are responsible for adhering to the prescribing standards set out in the NICE clinical guideline CG78, additional monitoring plans beyond the minimum as specified by NHFT Physical monitoring requirements.
- Ensuring that the guidance for the use of high dose antipsychotics is followed by the team
- Approving the tools use for estimating response and to be used for the patient monitoring
- Support patient during transition into a different type of care by ensuring all medication history and response are up to date and accurate

5.5. Medical / Non-Medical Prescribers/Team Doctors
- Undertaking the physical examination of in-patients.
- Provide appropriate information for patient and document consent in notes
- Ensuring that when patient is transferred, adequate information is transferred with the patient for continuity of care.
- Agree within team, an appropriate rating scale to be used for the individual, to rate the target symptoms, response and side-effects,
- Document the reviewed care plans and assessments on change of conditions

The current version of any policy, procedure, protocol or guideline is the version held on the NHFT internet. It is the responsibility of all staff to ensure that they are following the current version.
• Review continued use of high dose therapy where there is no clinical response to justify the medication and document in the electronic patient record.

• Ensuring that when patient conditions changes, the continue need for antipsychotic high dose are reviewed

• Undertake and record accurately the following investigations as soon as possible or on admission:
  • ECG
  • Weight (plotted on a chart)
  • Waist circumference
  • Pulse and blood pressure
  • Fasting blood glucose, glycosylated haemoglobin (HbA1c), blood lipid profile and prolactin levels
  • Blood tests to monitor the effects and side effects of medication, or as indicated by the medication regime
  • Assessment of any movement disorders

• Complete the risk factors (smoking, body mass index, glucose, lipids, blood pressure, alcohol) using the locally approved format

• Responding appropriately to the physical observation of patients. For example, patients and carers are to be made aware that they should report a raised temperature.

• Document the decision to prescribe high doses in the clinical notes along with a description of target symptoms.

• A Junior Doctor should only prescribe above the recommended dose following consultation with a consultant.

• A patient prescribed and administered PRN antipsychotic on a regular long term basis, should have a review with the intention of converting the antipsychotic dose to a regular dose.

• Record the rationale for continuing, changing or stopping medication, and the effects of such change

• Review progress referring to the target symptoms, response and side-effects identified at the start of treatment and repeating the rating scales where used.

• Reduce dose to within the licensed range if no significant progress is observed and consider alternatives, e.g. adjuvant therapy and newer or atypical antipsychotics such as clozapine.

• Continued use of high dose therapy where there is no clinical response should be justified in the Electronic patient record. Consultants should consider seeking a second opinion from a colleague.

• Ensure on patient’s discharge that GP and other relevant community mental health personnel are informed of high dose antipsychotic status and that required checks will continue to be performed by secondary care.
5.6. Unit Pharmacist:
- Provide assistance in helping with local monitoring of practices and leading on local and national audits to improve prescribing practices in the Trust.
- Identify that the patient is on high dose antipsychotics or has the potential for high dose when PRN medication is taken into account.
- Indicate on the patient’s drug chart and in the notes that a high dose regimen has been prescribed.
- Indicate on prescription chart the percentage of BNF maximum of each antipsychotic prescribed.
- Inform other staff and key workers of high dose status.

5.7. Nursing Staff (Registered and non registered):
- Assuring themselves that they have the necessary information on prescription is safe before administering.
- Undertake monitoring of Blood pressure, Pulse, Temperature, Hydration as requested by doctor.
- Aware of the potential of PRN antipsychotics to raise total daily dose of antipsychotic above high-dose threshold.
- Observe regularly as agreed, escalate out of range on any physical health concerns.
- Document all outcomes following assessment.
- Update the care plan in collaboration with the service user as soon as possible and prescribing of high dose antipsychotic.
- Documentation of response and side-effects, ideally using validated rating scales (e.g. Glasgow Atypical Side-effect Scale (GASS), Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS), Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression scale (CGI), should be standard practice so that there is ongoing consideration of the risk-benefit ratio for the patient.

5.8. Care co-ordinators:
- Support patient during transition into a different type of care by ensuring all medication history and response are up to date and accurate.

6. GUIDELINES FOR SE OF HIGH DOSE ANTIPSYCHOTICS

6.1. CIRCUMSTANCES UNDER WHICH HIGH DOSE CAN BE USED
High-dose prescribing either with a single agent or combined antipsychotics should rarely be used and then only for a time-limited trial in treatment resistant psychosis after all evidence-based approaches have been shown to be unsuccessful or inappropriate.

Adequate trials of standard treatment, (including clozapine for Schizophrenia) have been considered and decided against or have been tried and failed or...
terminated treatment due untoward side effect(s). Compliance has been assessed (e.g. drug assays, use of liquids) and not in doubt. Adjunctive e.g. mood stabilisers, antidepressants have been tried or considered not appropriate, including psychological approaches have failed or are not appropriate.

Clozapine has been considered not appropriate, or patient has been tried on clozapine Scientifically based combination of co-prescribing aripiprazole with other antipsychotics to reduce weight and normalise prolactin can sometimes be justified for as long as the patient had been tried on adequate doses of aripiprazole for sufficient time with no response. The maximum BNF dose must have been used consistently as prescribed for a period of up to three months as a minimum.

For acutely unwell patient on admission, the decision to increase dose beyond BNF maximum dose. For a dose increase for an acutely ill patient on admission, adequate time (usually 2-4 weeks at the recommended doses) to be allowed for response or to review target symptoms. The review period as agreed should be written on the medication chart and documented as part of the care plan.

The use of PRN antipsychotics resulting in high dose antipsychotic therapy should be avoided in all but the most exceptional circumstances. Where assessment of cardiovascular disease and status is difficult and ECGs impossible it is prudent to avoid high doses of antipsychotics, particularly parenterally.

6.2. Process to be undertaken when High dose regime is identified

Undertake baseline U&Es, FBC, LFTs, lipids, plasma glucose, prolactin, creatinine phosphokinase (CPK), BP, pulse, temperature, weight/BMI, prior to prescribing high dose or combination antipsychotics:
Also consider risk factors for increasing adverse effects
- old age,
- weight,
- renal and hepatic function,
- smoking status,
- concomitant drugs (particularly cardiotoxic drugs),
- known or suspected use of recreational drugs
- comorbidities (e.g. cardiac history- particularly MI or arrhythmias, family history of heart disease, diabetes, epilepsy, hepatic/renal impairment, alcoholism,
- minimal exercise tolerance,
- previous history of adverse reactions to high doses of antipsychotics.
In women, use lower doses than males and consider childbearing potential.

Consider drug interactions, particularly via CYP inhibition and those of established and well-documented clinical significance. Potentially hazardous combinations can arise even within standard doses. Avoid concomitant treatment with:

- terfenadine/astemizole
- diuretics
- anti-arrhythmics
- anti-hypertensives
- tricyclic antidepressants
- erythromycin
- citalopram

High-dose prescribing in pregnancy and women of child bearing potential requires careful assessment as dose related side effects may be of greater consequence in this patient group.

Ongoing consideration of the risk-benefit ratio for the patient should be planned into care to minimise any risks posed such potential to cause QTc prolongation, electrolyte disturbance or pharmacokinetic interactions via CYP inhibition.

Indicate on the drug prescription sheet and patient's recording notes that the patient is receiving high-dose antipsychotics.

Where possible, increase the dose slowly, ideally over intervals of at least one week.

Doses in excess of BNF maximum should be clearly specified for each drug on the appropriate Form T2/T3, stating an upper limit.

Ensure that High Dose Antipsychotic Monitoring form is completed on SystmOne. This form called ‘GEN - Anti-Psychotic Monitoring Form’ may be found in the Care Plans section under...
Psychiatric Rating Scale (BPRS), Clinical Global Impression scale (CGI) can be adopted provided the staff using them are trained to use them. This should be done at least once every three months and more frequently at start of high dose treatment. This should be done at least once every three months and more frequently at start of high dose treatment. This should be done at least once every three months and more frequently at start of high dose treatment. Where a patient’s ECG result is reported as borderline QTc (430–450ms for men or 440–460ms for women), be cautious as to using high dose antipsychotic and review treatment more regularly. Avoid using high dose where a prolonged QTc is recorded (over 450ms for men or over 470ms for women), consider changing medication and requesting a cardiology assessment. If the QTc is over 500ms stop suspected causative medicine(s) and refer to cardiologist immediately. It should be noted that there is no consensus between cardiologists regarding exact QTc ranges and prescribers should be guided by clinical factors.

6.3.1. Frequency of monitoring

ECG:
An ECG should be repeated after a few days and then every 1-3 months in the early stages of high-dose treatment and repeated as clinically indicated but at least 3 monthly whilst the high dose antipsychotic treatment continues and especially when there is history of cardiovascular disease and document reasons why it is decided to continue treatment with high dose antipsychotic in the patient’s record.

The monitoring of blood pressure, pulse, temperature, hydration status, urea and electrolytes and side-effects should be done at the following rate:
- BASELINE – Within a week of starting, or changing, anti-psychotics
- 6 WEEKS from starting, or changing, anti-psychotics
- 12 WEEKS from starting, or changing, anti-psychotics

6.4. CONSENT AND PATIENT INFORMATION

A multidisciplinary team member must have discussed with the patient and or patient’s advocate to obtain valid consent. Where it is deemed not possible or reasonable to obtain consent, this must be documented. Where a patient refused or unable to give his or her consent, follow the process as laid down by the Mental Capacity Act for an informal patient.

A thorough record of the decision and reasoning including target signs and symptoms and outcome should be discussed within the multidisciplinary team and documented.

For patients under the Mental Health Act 1983, Form T2 should be completed for patient’s consenting to high dose antipsychotic treatment and Form T3 after review by a Second Opinion Appointed Doctor (SOAD) for patients not consenting.
6.5. TRANSFER OF CARE
Where a formal referral to another sector of care, adequate communication of detailed plan
Send a copy of the care plan to the primary healthcare professional who made the referral and the service user

7. TRAINING

7.1. Mandatory Training
There is no mandatory training associated with this guideline

7.2. Specific Training not covered by Mandatory Training
Ad hoc training sessions based on an individual’s training needs as defined within their annual appraisal or job description. Information on this guideline is included within the Junior doctors induction training

8. MONITORING COMPLIANCE WITH THIS DOCUMENT

<table>
<thead>
<tr>
<th>Aspect of compliance or effectiveness being monitored</th>
<th>Method of monitoring</th>
<th>Individual responsible for the monitoring</th>
<th>Monitoring frequency</th>
<th>Group or committee who receive the findings or report</th>
<th>Group or committee or individual responsible for completing any actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of high dose antipsychotic medication and associated monitoring</td>
<td>Audit of prescription charts and associated patient records.</td>
<td>Medical Director</td>
<td>Bi-annual</td>
<td>Medicines Management Committee</td>
<td>Medicines Management Committee</td>
</tr>
</tbody>
</table>

Where a lack of compliance is found, the identified group, committee or individual will identify required actions, allocate responsible leads, target completion dates and ensure an assurance report is represented showing how any gaps have been addressed.

9. REFERENCES AND BIBLIOGRAPHY

1. Northamptonshire Healthcare NHS Foundation’s Physical Healthcare Policy CLP070


10. Report of the second round of the National Audit of Schizophrenia (NAS2) 2014


12. Summaries of product characteristics

13. National Audit Schizophrenia 2 (NAS 2), Royal College of Psychiatrists

10. RELATED TRUST POLICY

- MMP001 Control of Medicines Policy
- Physical Healthcare Policy (CLP070)
- Policy for Consent to Examination or Treatment (CLP016),
- Inpatient Admission Policy,
- Guideline for the management of antipsychotic-induced hyperprolactinaemia (MMG007).
- Primary Thromboprophylaxis for patient admitted to NHFT (MMP016)
- CLP049: Standard for Minimum Level of Physical Examinations
APPENDIX 1 – IDENTIFICATION OF PATIENTS ON HIGH-DOSE ANTIPSYCHOTIC MEDICATION

High dose antipsychotic prescribing may be achieved in TWO ways:

A. Single antipsychotic drug prescribed at a daily dose above the BNF upper recommended limit (High-dose single drug)

B. More than one antipsychotic prescribed concurrently (High-dose through the prescribing of multiple drugs)

N.B. In defining what constitutes a high-dose of antipsychotics for patients receiving more than one antipsychotic at doses within the normal BNF ranges, it is probably most satisfactory to add the percentages of the patient’s current dose of antipsychotic expressed as a percentage of the recommended upper dose for each antipsychotic. Where this equals or exceeds 100%, the patient is considered to be receiving a ‘high-dose’.

For example: a patient on zuclopenthixol depot 300mg weekly and olanzapine 15mg daily: Sum of percentages: 50% + 75% = 125% (>100% therefore high-dose)

<table>
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<tr>
<th>ANTIPSYCHOTIC</th>
<th>MAXIMUM LICENSED DAILY DOSE i.e. 100% (mg/day)</th>
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<tbody>
<tr>
<td></td>
<td>Orally</td>
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<tr>
<td>Amisulpride</td>
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<td>Aripiprazole</td>
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Use of AS REQUIRED antipsychotic medication must also be taken into account.

The current version of any policy, procedure, protocol or guideline is the version held on the NHFT internet. It is the responsibility of all staff to ensure that they are following the current version.

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