MMG012 GUIDELINES FOR THE USE OF HIGH DOSE ANTIPSYCHOTIC MEDICATION
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Why we need this Policy
There is limited evidence for the use of antipsychotics above the licensed dose range. The majority of adverse effects caused by antipsychotics, such as postural hypotension, anticholinergic and extrapyramidal side effects are dose related. Combining antipsychotics has also been associated with longer hospital stays and more frequent adverse effects.

High dose antipsychotics should only be used in exceptional circumstances and the decision to do so should be made by a senior psychiatrist.

A high dose regime is defined as:

- The use of a single antipsychotic above the recommended maximum dose
- The use of two or more antipsychotics where the sum total percentage exceeds 100% of the BNF recommended dose

The Northamptonshire Healthcare NHS Foundation Trust’s (NHFT) clinical policy; Standard for Minimum Level of Physical Examination (CLP049)\(^2\) defines the level of physical health standard required for patients according to their lifestyle, medication and co-morbid conditions. The NHFT Physical Healthcare Policy (CLP070)\(^3\), highlights that all healthcare staff are bound by the duty of care to ensure that all patients cared for by the Trust receive a minimum standard of physical healthcare.

What the Policy is trying to do
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.

Which stakeholders have been involved in the creation of this Policy
Medicines Management Committee 17/05/16
Clinical Directors and Lead Clinicians-General adult
Any required definitions/explanations

- 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
- PRN – as required (Pro Re Nata – Latin)
- GASS – Glasgow Atypical Side-effect Scale
- LUNERS – Liverpool University Neuroleptic Side Effect Rating Scale
- BPRS – Brief Psychiatric Rating Scale
- CGI – Clinical Global Impression scale
- BMI – Body Mass index
- BP – blood pressure
- NMS – Neuroleptic Malignant Syndrome
- CPK – Creatinine Phosphokinase
- MI – Myocardial Infarction
- CYP – Cytochrome P
- BNF – British National Formulary

See Appendix 1 for maximum daily doses of antipsychotics as recommended by the (BNF)
Key duties

Medicines Management Committee

- Will approve and review these guidelines, and commission regular audit of treatment to check that the guidelines are being followed and used appropriately

Medical Director

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

Clinical Directors

- 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

Responsible Clinicians/ Consultant Psychiatrists

- Hold the sole responsibility to prescribe high dose antipsychotic or a combination of more than one antipsychotic over a specified trial period
- To obtain informed consent from patient before prescribing high dose antipsychotics wherever possible and document this in the patients electronic medical notes
- Are responsible for adhering to the prescribing standards set out in the NICE clinical guideline CG78 and additional physical health monitoring beyond the minimum as specified by NHFT Physical monitoring requirements.
- Ensuring that the guidance for the use of high dose anti psychotics is followed by the team
- Ensure patients medication history as well response to previous treatments are up-to-date and recorded in the patients electronic medical records.

Medical / Non-Medical Prescribers/Team Doctors

- Undertaking the physical examination of in-patients.
- Provide appropriate information regarding high dose antipsychotics 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,

• Where a patient’s condition changes, review and document care plans and assessments in patients electronic notes

• Review regime regularly and establish if there is an improvement in clinical presentation in response to high dose antipsychotics. Where there is no improvement or response the rationale for continuation of high dose antipsychotics must be recorded in the patients’ electronic medical records and a second opinion should be sought.

• Undertake and record the following investigation on initiation of high dose antipsychotic regimen:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>U&amp;Es</td>
<td>Baseline and yearly as part of a routine physical health check</td>
</tr>
<tr>
<td>FBC</td>
<td>Baseline and yearly as part of a routine physical health check</td>
</tr>
<tr>
<td>Blood lipids</td>
<td>Baseline, at three months then yearly</td>
</tr>
<tr>
<td>Weight</td>
<td>Baseline, frequently for three months</td>
</tr>
<tr>
<td>Plasma glucose</td>
<td>Baseline, at 4-6 months then yearly (fasting blood glucose and glycosylated haemoglobin (HbA1c)</td>
</tr>
<tr>
<td>ECG</td>
<td>Baseline and after dose changes, on admission and before discharge if drug regimen changed</td>
</tr>
<tr>
<td>BP and Pulse</td>
<td>Baseline and frequently (minimum of daily whilst in an inpatient setting) during titration</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Baseline, then at 6 months, then yearly</td>
</tr>
<tr>
<td>LFTs</td>
<td>Baseline and yearly as part of a routine physical health check</td>
</tr>
<tr>
<td>CPK</td>
<td>Baseline, then if NMS suspected</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Assess movement disorders</th>
<th>Baseline and regularly during treatment</th>
</tr>
</thead>
</table>

- Complete the risk factors (smoking, BMI, glucose, lipids, blood pressure, alcohol) using the physical health monitoring template on SystmOne patient notes. Making patients and carers aware of any changes in physical health that need to be reported, such as raised temperature, and respond appropriately.

- 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 the consultation with a consultant.

- A patient prescribed and administered PRN antipsychotic on a regular 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 repeat the use of rating scales if originally 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.

- 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.

**Ward Pharmacist:**

Provide guidance on prescribing and monitoring requirements with regards to high dose antipsychotics regimes.

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 (regular and PRN).

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Inform other staff and key workers of high dose status

Nursing Staff (Registered and non-registered):

Ensure medication has been prescribed correctly before administering medication to patient

Undertake monitoring of BP, pulse, temperature hydration and nutritional status as requested by doctor

Be aware of the potential of PRN antipsychotics to raise total daily dose of antipsychotics above high-dose threshold.

Regularly monitor and record physical health as agreed with prescriber and escalate any concerns immediately

Update the care plan in collaboration with the service user as soon as possible after high dose antipsychotics have been prescribed

Documentation of response and side-effects, ideally using validated rating scales (e.g. GASS, LUNSERS, BPRS and CGI),

Policy detail

Guidelines for use of High dose antipsychotics

Circumstances Under Which High Dose Regimens Can Be Use

High-dose prescribing either with a single agent or combined antipsychotics should not be used routinely and if commenced, high dose regimens should only be used 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 treatment has been stopped due to adverse side effect(s).

Noncompliance has been assessed (e.g. drug assays, use of liquids) and ruled out.

Adjunctive treatments such as mood stabilisers, antidepressants as well as psychological approaches have been tried or considered to be inappropriate.
Where Clozapine has been considered inappropriate or ineffective or where the addition of another antipsychotic has been shown to reduce side effects. There is evidence to suggest that the addition of Aripiprazole reduces prolactin levels and prevents weight gain.

The use of PRN antipsychotics resulting in high dose antipsychotic therapy should be avoided in all but the most exceptional circumstances.

High dose antipsychotics, particularly via the parental route, should be avoided if an ECG as well as assessment of cardiovascular risk cannot be undertaken.

**Process to be undertaken when High dose regime is identified**

On commencement of high dose antipsychotic regimes, a discussion must take place to inform patients of the rationale behind prescribing high dose antipsychotics and this must be recorded in the patient’s electronic notes.

High dose antipsychotic must be indicated on the front of the inpatient chart.

Undertake the following baseline monitoring prior to prescribing high dose or combination antipsychotics: U&E’s, FBC’s, LFT’s, lipids, plasma glucose, prolactin, creatinine phosphokinase (CPK), BP, pulse, temperature, weight/BMI,

Also consider risk factors for increasing adverse effects

- age (increased risk in elderly patients)
- 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

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- anti-arrhythmics
- anti-hypertensives
- tricyclic antidepressants
- erythromycin
- citalopram

Regular review and consideration of risks (such as QTc prolongation, electrolyte disturbance and pharmacokinetic interactions) versus benefits should be undertaken and recorded in the patients care plan.

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 T2/T3 form, stating an upper limit.

Ensure that the Physical Health Monitoring template is completed which can be found on SystmOne. This form also contains a section where High Dose Antipsychotic doses must be recorded.

**Prescribing in pregnancy**

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.

**Monitoring requirements for patients on High dose Antipsychotic regimes**

See section for monitoring parameters on initiation and during treatment

In addition to meeting the standard minimum level of physical examination for in-patient, the specified requirements as set by the Trust physical healthcare policy (Physical Healthcare Policy CLP070) is adequate for most patients prescribed high dose antipsychotics for the duration of 12 months or until care can be transferred to the primary care.

Other patient groups that may need more detailed monitoring, if high-dose prescribing is considered, include: older adults (aged 65 years or over, excluding patients diagnosed with dementia), child and adolescents, those known or suspected to use recreational substances and patients (aged under 18 years) with significant comorbidities.

Validated rating scales such as Glasgow Atypical Side-effect Scale (GASS), Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS), Brief 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.

Where a patient’s ECG result is reported as borderline QTc (430–450ms for men or 440–460ms for women), be cautious when prescribing high dose antipsychotic and review treatment more regularly. Consider antipsychotics less likely to prolong QTc and consider more frequent ECGs.
Avoid using high dose where a prolonged QTc is recorded (over 460ms for men or over 480ms 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.

**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, antipsychotics
- **6 WEEKS** from starting, or changing, antipsychotics
- **12 WEEKS** from starting, or changing, antipsychotics

**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:

- Complete/update T2 form for patient’s consenting to high dose antipsychotic treatment
- Complete/update T3 form after review by a Second Opinion Appointed Doctor (SOAD) for patients not consenting.

**TRANSFER OF CARE**

Where a patient moves between inpatient, community or between sectors within the trust (as well as when care is shared with GPs) detailed information regarding the patients care must be communicated correctly.

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Training requirements associated with this Policy

Mandatory Training

There is no mandatory training associated with this guideline

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.

How this Policy will be monitored for compliance and effectiveness

<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.
For further information

- MMP001 Control of Medicines Policy

Equality considerations

- See MMP001 Control of Medicines Policy

Reference Guide

- Northamptonshire Healthcare NHS Foundation Trust Clinical Policy. Standard for Minimum Level of Physical Examination (CLP049)
- Northamptonshire Healthcare NHS Foundation’s Physical Healthcare Policy CLP070
- Consensus Statement on the Use of High Dose Antipsychotics. The Royal College of Psychiatrists. May 2006
- Report of the second round of the National Audit of Schizophrenia (NAS2) 2014
- Summaries of product characteristics
- National Audit Schizophrenia 2 (NAS 2), Royal College of Psychiatrists

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## Document control details

<table>
<thead>
<tr>
<th>Version No.</th>
<th>Date Ratified/Amended</th>
<th>Date of Implementation</th>
<th>Next Review Date</th>
<th>Reason for Change (e.g. full rewrite, amendment to reflect new legislation, updated flowchart, minor amendments, etc.)</th>
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<tbody>
<tr>
<td>V0.01</td>
<td>May 2016</td>
<td>May 2016</td>
<td>May 2018</td>
<td>Minor amendments</td>
</tr>
<tr>
<td>V0.02</td>
<td>May 2018</td>
<td>May 2018</td>
<td>May 2020</td>
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</table>

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Appendix 1
Maximum daily doses of antipsychotics
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>
<thead>
<tr>
<th>ANTIPSYCHOTIC</th>
<th>ADULT MAXIMUM LICENSED DAILY DOSE i.e. 100% (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Orally</td>
</tr>
<tr>
<td>Amisulpride</td>
<td>1200</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>30</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>1000</td>
</tr>
<tr>
<td>Benperidol</td>
<td>1.5</td>
</tr>
<tr>
<td>Clozapine</td>
<td>900</td>
</tr>
<tr>
<td>Flupentixol</td>
<td>18</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug</th>
<th>BNF Max</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluphenazine</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Pericyazine</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>Pimozide</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>100</td>
<td>75</td>
</tr>
<tr>
<td>Promazine</td>
<td>800</td>
<td>100</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>750</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Sertindole</td>
<td>24</td>
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</tr>
<tr>
<td>Sulpiride</td>
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<td></td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Zotepine</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>Zuclopenthixol</td>
<td>150</td>
<td></td>
</tr>
</tbody>
</table>

**Depot Prescriptions**

<table>
<thead>
<tr>
<th>Drug</th>
<th>BNF Max and Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flupentixol Decanoate</td>
<td>400mg weekly</td>
</tr>
<tr>
<td>Fluphenazine Decanoate</td>
<td>100mg 2 weekly</td>
</tr>
<tr>
<td>Haloperidol Decanoate</td>
<td>300mg 4 weekly</td>
</tr>
<tr>
<td>Pipothiazine Palmitate</td>
<td>200mg 4 weekly</td>
</tr>
<tr>
<td>Risperidone</td>
<td>50mg 2 weekly</td>
</tr>
<tr>
<td>Zuclopenthixol Decanoate</td>
<td>600mg weekly</td>
</tr>
<tr>
<td>Clopixol Acuphase</td>
<td></td>
</tr>
<tr>
<td>Zuclopenthixol Acetate</td>
<td>400mg total over 2 weeks</td>
</tr>
</tbody>
</table>

Use of AS REQUIRED antipsychotic medication must also be taken into account.