East London NHS Foundation Trust

Policy for the use of high dose antipsychotic medication

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6.0	August 2014	Amendment to policy to reflect changes to BNF maximum doses for oral and intramuscular haloperidol. Amendment to high dose monitoring tool. Update of antipsychotic dosage reckoner.
7.0	August 2016	Amendment to high dose monitoring tool. Update of antipsychotic dosage reckoner

Policy for the use of high-dose antipsychotic medication

1.0 Introduction

1.1 The purpose of this policy is to provide clear guidance on matters related to the use of high-dose antipsychotic medication in in-patients and community patients

1.2 ***The policy protects the right to treatment of patients who do require higher doses for effective treatment. For this, each patient should be assessed carefully by a fully trained psychiatrist.***

1.3 Unless otherwise stated, doses in the BNF are licensed doses – any higher dose is therefore **off-license**. The prescribing of licensed medicines outside the recommendations of the Marketing Authorisation alters (and probably increases) the doctor's professional responsibility.

1.4 The decision to raise the total dose of antipsychotics above the recommended upper limit must be taken by a Consultant Psychiatrist only.

1.5 As stated in the Trust Medicines Policy, nurses administering doses of antipsychotics above BNF maximum doses must check the case notes for the rationale behind this decision and confirmation of dose.

1.6 This document is made in conjunction with the 'Consensus statement on high-dose antipsychotic medication', from The Royal College of Psychiatrists, the November 2014 version[5]

1.7 Definition of High Dose Antipsychotic Therapy (HDAT)

1.7.1 Single antipsychotic drug prescribed at a total daily dose exceeding the recommended BNF upper limit/ the manufacturers Summary of Product Characteristic (SPC)

Or

1.7.2 More than one antipsychotic prescribed concurrently.

This is assessed by adding together the doses of each drug expressed as a percentage of their respective BNF maximum dose and where this exceeds 100%, the patient is considered to be receiving a "high-dose".

1.7.3 *For example*:

Zuclopenthixol depot 300mg weekly (50%) and Olanzapine 15mg daily (75%) = 50% + 75% = 125% (>100%, therefore 'high dose')

1.7.4 'As required' antipsychotics contribute to HDAT.

For example

Olanzapine 20mg daily (100%) and haloperidol 5mg BD "as required" (50%) = 100% + 50% = 150%

Recommendations

Two or more antipsychotic drugs should only be given concurrently as part of a considered treatment plan.

- The use of more than one antipsychotic may cause increased adverse effects
- The use of more than one antipsychotic is associated with increased mortality
- The evidence-base supporting the use of more than one antipsychotic or higher than recommended maximum doses is poor.
- The benefit of using more than one antipsychotic must out weigh the risk of using high dose antipsychotic regimes
- The use of high dose antipsychotic therapy to be considered after several evidence based adequate trials of antipsychotic monotherapy including clozapine have failed[5]
- A trial of high dose antipsychotic therapy must be carefully monitored
- Supplementary prescribers should not take the decision to prescribe high dose antipsychotics

Guidelines for the Co-Prescription of Antipsychotics

1. Where ever possible one antipsychotic should be prescribed.

2. If no response is seen after 6 to 8 weeks at a therapeutic dose the antipsychotic should be switched to another antipsychotic. At this stage, it is imperative that compliance with the first drug has been checked thoroughly and verified.

3. Where no response is seen with the second antipsychotic, either consider switching to clozapine (as per NICE guidance) or to a third antipsychotic.

4. If there is no response or a lack of tolerance to the third antipsychotic or clozapine, consider adding in a second antipsychotic.

5. Before the second antipsychotic is prescribed, baseline Brief Psychiatric Rating Scale (BPRS) should be performed and the reason for co-prescription clearly documented in the notes.

6. A second BPRS should be performed 6-8 weeks after baseline and if there is no improvement in mental state, the withdrawal of the second drug should be considered.

2.0 The Policy

2.1 All treatment areas including In-patient, Community Mental Health Teams (CMHT's) and Specialist Services such as Early Intervention and Day Services must have a copy of the policy available. All staff that will be involved with high-dose antipsychotic medication must be confident to operate within the policy.

3.0 Alternatives strategies to high-doses of antipsychotics

3.1 Emergencies

3.1.1 In emergency, use rapid tranquilisation regime – see Trust Rapid Tranquilisation Guidelines for Adult, Older people or CAMHS.

3.2 Acute Treatment

3.2.1 In acute treatment, it is recommended that the dose of medication should be increased only gradually, e.g. weekly, so as not to exceed the dose needed to treat the psychosis. Any antipsychotic effects may take 1-2 weeks to become evident. Increasing the dose slowly is also thought to reduce the risk of neuroleptic malignant syndrome. If the patient is responding slowly and there is some urgency in the clinical situation, other methods of inducing a remission should also be considered.

3.3 When Required Medication

3.3.1 The use of PRN medication should be reviewed regularly and should include training for the clinical team on its use and alternative strategies. Staff should be aware of the potential for PRN medication to raise the total daily dose of antipsychotic above the high dose threshold.

3.4 Treatment Failure

3.4.1 For patients who have failed to respond to two antipsychotics at full dose, consider the following[1]:

3.4.2 Review the diagnosis. Consider organic causes, and illicit drug use.

3.4.3 Consider therapeutic drug levels, and compliance.

3.4.4 Has sufficient time been allowed for response to take place?

3.4.5 Consider reducing the antipsychotic dose slowly for a trial period. Some studies suggest a curvilinear dose response relationship, possibly because of inducing iatrogenic negative symptoms at very high dose. Rarely the anticholinergic effects of the antipsychotics may induce a toxic psychosis which will improve with dose reduction[3].

3.4.6 Consider adverse social and psychological factors which may be perpetuating the psychosis, including family factors, or if In-patient the ward environment and disturbances caused by other patients.

3.4.7 Consider specific psychological interventions aimed at target symptoms such as hallucinations or at improving the level of social role functioning, i.e. rehabilitation.

3.4.8 Consider other treatments such as mood stabilisers, or antidepressants, if there are severe mood symptoms, agitation or overexcitement.

3.4.9 Consider clozapine in treatment resistant patients i.e. those patients who have shown no or little response to at least two different antipsychotics.

Before combination antipsychotics are used, specific actions should be taken to ensure:

- The diagnosis is correct
- Treatment dose and duration has been adequate
- Plasma levels (if appropriate) are therapeutic and concordance with treatment ensured
- Alternative adjunctive drug therapies have been tried

Appropriate indications for use of more than one antipsychotic include:

- Rapid Tranquilisation (see trust rapid tranquilisation guidelines)
- Failed or partial response to clozapine
- Neutropenia or agranulocytosis with clozapine
- When switching from one antipsychotic to another (6 weeks crossover)
- As a temporary measure with depot medication during an acute exacerbation of illness

- **Inappropriate indications would include:**
- Failure to wait an adequate length of time for the first drug to have a full antipsychotic effect (6 months for clozapine, 6 weeks for all other oral antipsychotics and 8 weeks for depot medication)
- Where clinical improvement occurs before a switch of antipsychotics is completed
- Where patient is possibly treatment resistant and clozapine has not been tried
- Where benefit (as assessed by rating scales) does not outweigh the risk

4.0 Recommendations for high-dose antipsychotic prescribing

4.1 Discuss the reasons for the treatment, and consideration of alternatives, with the multidisciplinary team, and if possible the patient and their family or advocate.

4.2 Consider dose-related adverse reactions, and cumulative adverse reactions.

4.3 Obtain 'real or proper' consent where possible, and for detained patients ensure compliance with the provisions of part IV of the Mental Health Act 1983.

4.4 Consider a second opinion, or discuss with another consultant psychiatrist.

4.5 In-patient prescription sheets and community charts where appropriate must indicate when a patient is receiving high dose antipsychotic.
When high dose antipsychotics are prescribed for In-patient a 'HIGH DOSE ANTIPSYCHOTICS SHEET' (SEE Appendix One) IS attached to the drug chart and must be completed by SHO. On discharge a copy is sent to GP and original filed in patient's notes. For patients in community prescribed high dose antipsychotics the prescriber is responsible for completing form and notifying the GP. Form should be attached in patients notes.

4.6 Increase the dose of antipsychotic(s) slowly.

4.7 Patient's progress should be reviewed at least 3 monthly and the dose reduced to within the licensed range if no significant progress is observed and alternatives considered.

4.8 Formal mental state examination eg. Brief Psychiatric Rating Scale (BPRS), should be performed at baseline, six and 12 weeks and then three monthly thereafter. If no clinical improvement is seen after six to eight weeks (change of at least 20% in BPRS score), consider reducing the dose.

4.9 Continued use of high dose therapy where there is no clinical response should be justified in the patient's medical notes.

4.10 A second medical opinion (formal for detained patients or in-house if informal) should be obtained for patients taking 'high dose' antipsychotics.
It is the responsibility of the consultant to ensure all monitoring is done according to the policy.
Community based patients should be monitored by consultant or by GP if there is an agreed shared care.

5.0 High risk patients and high-dose antipsychotic prescribing

5.1 Cardiac disorder, tobacco and alcohol use, obesity, illicit drug use, impaired glucose tolerance, diabetes, patients taking any drug which may lower the seizure threshold, hepatic or renal impairment and old age should be taken into consideration when starting a patient on high-dose antipsychotic medication.

6.0 Potential drug Interactions for high-dose antipsychotic prescribing

6.1 Consider potential Pharmacodynamic (additive) side effects as well as pharmacokinetic ones e.g. risperidone may inhibit the metabolism (and therefore increase levels) of certain antipsychotics and other psychotropic drugs.

6.2 Refer to current edition of BNF, or contact Medicines Information Centre, Pharmacy Department.

7.0 Mandatory monitoring for high-dose antipsychotic prescribing

7.1 Baseline ECG and then repeated periodically (minimum 3 monthly during initiation phase). If QTc is prolonged **(>440ms for men; >470msec for women)** or other adverse abnormality develops, treatment should be reviewed and cardiology assessment considered.

7.2 Monitor blood pressure, pulse, temperature and (by physical examination and/or urea and electrolytes, weekly initially. Consider extending monitoring interval to yearly when treatment is stable or none of the listed risk factors present
(refer to 5.1 or HDA monitoring tool).

7.3 Monitor urea and electrolytes minimum 3 monthly initially is suggested as additional monitoring.

7.4 Monitor for side effects using either LUNSERS (Liverpool University Neuroleptic Side Effect Rating Scale or GASS (Glasgow Antipsychotic Side Effect Scale)for second generation antipsychotics.

7.5 Monitor patients for improvement in psychotic symptoms with BPRS or PANSS (Positive and Negative Symptom Score)

8.0 Resuscitation

8.1 All psychiatrists should have experience in resuscitation and know how to use the resuscitation equipment in the hospital. Each ward should have an appropriate procedure for dealing with cardiac arrest.
In the event of a cardiac arrest in community dial 999 and initiate basic life support. Click on link Resuscitation Policy

8.2 All sudden unexpected deaths which might be associated with antipsychotic prescribing should be reported using the yellow card scheme.

9.0 Antipsychotics – Dose Percentage Conversion Table

Oral Doses mg/day	20%	25%	33%	40%	50%	67%	75%	80%	100%
TYPICALS									
Benperidol			0.5mg		0.75mg	1mg			1.5mg
Chlorpromazine	200mg	250mg	330mg	400mg	500mg	660mg	750mg	800mg	1000mg
Flupenthixol			6mg		9mg	12mg			18mg
Haloperidol		5mg			10mg		15mg		20mg
Levopromazine	200mg	250mg			500mg		750mg		1000mg
Pericy azine		75mg	100mg		150mg	200mg			300mg
Promazine	160mg	200mg			400mg		600mg		800mg
Sulpiride	400mg	600mg	800mg		1200mg	1600mg	1800mg		2400mg
Trifluoperazine*	10mg			20mg	25mg				50mg
Zuclopenthixol	30mg		50mg	60mg	75mg	100mg			150mg
ATYPICALS	20%	25%	33%	40%	50%	67%	75%	80%	100%
Amisulpiride	240mg	300mg	400mg	480mg	600mg	800mg	900mg	960mg	1200mg
Aripiprazole			10mg		15mg	20mg			30mg
Asenapine		5mg			10mg		15mg		20mg
Clozapine	180mg	225mg	~300mg	360mg	450mg	600mg	675mg	720mg	900mg
Lurasidone		37mg			74mg		111mg		148mg
Olanzapine		5mg			10mg		15mg		20mg
Paliperidone		3mg			6mg		9mg		12mg
Quetiapine *(Schizophrenia)*	150mg				375mg				750mg
Quetiapine *(Mania)*		200mg			400mg		600mg		800mg
Risperidone		4mg			8mg		12mg		16mg
INTRAMUSCULAR INJECTIONS (I.M) mg/day	20%	25%	33%	40%	50%	66%	75%	80%	100% Daily Dose
Aripiprazole			10mg		15mg	20mg			30mg
Haloperidol		3mg			6mg				12mg
Loxapine (inhaled)					5mg				10mg
Olanzapine		5mg			10mg		15mg		20mg
Zuclopenthixol Acetate (Clopixol Acuphase)	Maximum Cumulative Dose = 400mg in 2 week period Maximum 4 injections. Maximum of 150mg in 48 hours or 75mg in 24 hours								75mg
DEPOTS/ LONG ACTING INJECTIONS (LA) mg/week	20%	25%	33%	40%	50%	67%	75%	80%	100% Weekly Dose
Flupenthixol Decanoate	80mg	100mg			200mg		300mg		400mg
Fluphenazine Decanoate		12.5mg			25mg		37.5mg		50mg
Haloperidol decanoate			25mg		37.5mg	50mg			75mg
Olanzapine Embonate (LA)					75mg				150mg
Paliperidone palmitate						25mg			37.5mg
Pipotiazine Palmitate		12.5mg			25mg		37.5mg		50mg
Risperidone consta (LA)					12.5mg		18.75mg		25mg
Zuclopenthixol Decanoate		150mg	200mg		300mg	400mg	450mg		600mg

* There is no maximum dose for trifluoperazine stated in BNF/SPC; 50mg is used by convention

Table adapted from POMH-UK "*Antipsychotic Dosage Reckoner version 6: Mar 2015*

Responsibilities

Pharmacist Responsibilities:

- Identify that a patient is on high-dose antipsychotics
- Complete patient details on high dose antipsychotic therapy (HDAT) sheet
- Complete high-dose details and write % of maximum antipsychotic dose being prescribed (see section 1.6.3)
- Check that monitoring sheet is being completed
- Complete interacting medicines section
- Inform consultant, named nurse and care co-ordinator of high-dose status

Junior Doctor Responsibilities

- Fill in Risk Factors
- Order ECGs
- Check U&Es
- Check LFTs
- Document BPRS scores
- Document reason for high-dose in case notes
- Inform patient and document consent in notes
- Check that monitoring sheet is being completed
- Check high dose antipsychotic therapy (HDAT) is mentioned on consent to treatment or second opinion form, if applicable
- Ensure on patients' discharge that GP and other relevant community mental health personnel are informed of HDAT status and required checks.
- Ensure a system by which the required tests and reviews will be conducted and is agreed with the relevant community mental health personnel & / or GP.

Nursing Staff Responsibilities

- Temperature check
- Blood pressure check
- Document "high dose" status in the nursing care plan and daily progress notes.
- Check that monitoring sheet is being completed
- Ensure that high-dose status is discussed at review

Consultant Responsibilities

- Ensure policy is followed for HDAT
- Monitor Community based patients as per policy
- Use of high-dose antipsychotic therapy is solely the responsibility of the consultant.

Non-Medical Prescribers (NMP)

- Non-Medical Prescribers should not make the decision to proceed with the use of high dose medication.
- Use of high-dose antipsychotic therapy is solely the responsibility of the consultant

References

1 *Royal College of Psychiatrists Consensus statement on the Use of High Dose Antipsychotic Medication, Council Report CR190 November 2014*

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5 Central and North West London NHS Foundation Trust(For Adults), 2009, High Dose *Antipsychotic Policy.*

6 Bradford District Care NHS Trust, Guidelines for the Use of High Dose Antipsychotic Medication, May 2009.

7 Birmingham and Solihull Mental Health NHS Foundation Trust, Clinical Guideline: The Prescribing of High Dose and combination Antipsychotic Medication, Sep 2010

8**. POMH-UK** "Antipsychotic Dosage Reckoner version 6 Mar 2015.

9 www.bnf.org accessed 9/08/2016.

10. Taylor D, Paton C, Kapur S: Maudsley Prescribing Guidelines in Psychiatry 12th Edition, 2015, WILEY Blackwell.

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HIGH DOSE ANTIPSYCHOTIC THERAPY (HDAT) MONITORING SHEET

To be completed for all high dose antipsychotic therapy patients – preferably before commencing treatment.

Patient name:	**Gender:**	**Hospital Number:**
Ward/ Community Team:		**Consultant:**

- Inpatients – Undertake monitoring at baseline and at regular intervals including after dose changes (minimum every three months)
- Community patients – Continue monitoring at regular intervals, consider minimum once per year if patient maintained on stable dose of antipsychotic
- QTc Interval: (Abnormal >440msec men; >470msec women) **If prolonged contact cardiologist for advice, document in clinical notes**
- Temperature and Blood Pressure to be monitored weekly when inpatient. See NEWS chart.

High Dose Antipsychotic Therapy								
Date of high dose prescription:								
Specify antipsychotic drug(s), dose(s) & frequencies.								
Reason for HDAT prescription								
Pharmacist complete % antipsychotic dose								
Potential drug interactions? Y/N (if yes, give details)								
	Date Due:	**Date Completed:**	**Date Due:**	**Date Completed:**	**Date Due:**	**Date Completed:**	**Date Due:**	**Date Completed:**
ECG (date and QTc msec)								
U&Es (✓& date if OK)								
LFTs (✓& date if OK)								
Medication Review & date								
BPRS/PANSS Scores								
Name & title of person completing form								