Guidance on the Use of High Dose Antipsychotic Treatment (HDAT)

Key messages:

- **The use of high dose antipsychotics is "off-label" and should be exceptional clinical practice, only employed when an adequate trial of standard, evidence-based treatments, have failed or been otherwise excluded (including clozapine).**
- **Documentation of target symptoms, response and side-effects, ideally using validated rating scales (e.g. BPRS, LUNSERS), should be standard practice so that there is ongoing consideration of the risk benefit ratio for the patient. Rigorous physical monitoring (including ECG) is essential**

Definition of HDAT

High dose antipsychotic treatment results from the prescription of either:

1. A single antipsychotic in a total daily dose which exceeds the recommended maximum dose stated in the Summary of Product Characteristics (SPC) or BNF (see table below);

OR

2. Two or more antipsychotics (including cross-tapering) which, when expressed as a percentage of their respective recommended maximum doses stated in the SPC or BNF and added together, result in a cumulative dose of >100% [N.B. the calculation should include current prescriptions for all regular and "as required" (PRN) antipsychotic medication]

For example:
- a patient is prescribed zuclopenthixol depot 300mg weekly and olanzapine 15mg daily.
- sum of percentages = 50% (zuclopenthixol) + 75% (olanzapine) = **125%**, i.e. "high dose"

ANTIPSYCHOTIC	MAXIMUM LICENSED ADULT DOSE i.e. 100% Recommended doses for the elderly are shown in brackets
Oral	**mg per day**
Amisulpride	1200
Aripiprazole	30
Chlorpromazine	1000 (500)
Clozapine	900
Flupentixol	18
Haloperidol	20
Lurasidone	148
Olanzapine	20
Quetiapine **(Mania)**	800
Quetiapine **(Schizophrenia)**	750
Paliperidone	12
Risperidone	16 (4)
Sulpiride	2400
Trifluoperazine*	50
Zuclopenthixol	150
Injections	**mg per day**
Haloperidol	12
Zuclopenthixol acetate ["Acuphase"]	150 (100) maximum cumulative dose 400mg per course and maximum 4 injections
Depots/LA Injections	**mg per week**
Aripiprazole	100
Flupentixol decanoate ["Depixol"]	400
Fluphenazine decanoate	50
Haloperidol decanoate	75
Olanzapine	150
Paliperidone	37.5
Risperidone	25
Zuclopenthixol decanoate ["Clopixol"]	600
* max dose not stated by manufacturer Refs: BNF No 70 and Maudsley Guidelines 12th edition (2015)	

Efficacy

- There is no firm evidence that high doses of antipsychotics are any more effective than standard doses, for any clinical indication
- All currently available antipsychotics (with the possible exception of clozapine) exert their effect primarily through antagonism (or partial agonism) at post-synaptic dopamine receptors. There is increasing evidence that in some patients with schizophrenia, symptoms do not seem to be driven through dysfunction of dopamine pathways; so increasing dopamine blockade in such patients is futile.

Adverse effects

The majority of side-effects associated with antipsychotics are dose-related, including extrapyramidal side effects (EPSE), sedation, postural hypotension, anticholinergic effects, QT prolongation and sudden cardiac death. Thus, high dose antipsychotic treatment would be expected to worsen the incidence and severity of adverse effects.

Before prescribing HDAT

Ensure that:

- Sufficient time has been allowed for a response to standard dose treatment;
- At least two different antipsychotics have been tried sequentially;
- Clozapine has been considered / failed / not tolerated / refused or is contra-indicated;
- Compliance with treatment is not in doubt;
- Adjunctive medications (e.g. antidepressants, mood stabilisers) are not indicated;
- Psychological interventions have failed or are not appropriate
- The patient's physical health status has been considered and they are likely to tolerate HDAT

Decision to prescribe HDAT:

- The decision should be taken by a level ST4 doctor or above with membership of the Royal College of Psychiatrists and should involve completion of an individual risk/benefit assessment.
- The decision should involve consultation with the wider clinical team, the patient, any family if relevant or involved in patient consent, and with a patient advocate (if the patient wishes). Patient consent should be gained if they have capacity to provide this; if they do not have capacity, and HDAT is considered to be in their best interests, a second opinion should be sought.
- The decision to prescribe HDAT and the associated patient capacity and/or consent should be documented in the case notes, including the assessment of risks and benefits, the aims of treatment and plans for assessment of response and outcome.
- A decision by a doctor below ST4 to prescribe additional antipsychotic treatment for a patient admitted out-of-hours, which results in HDAT, must be reviewed by an ST4 doctor or above by the end of the next working day.

PROCEDURE TO FOLLOW ONCE THE DECISION TO PRESCRIBE HDAT HAS BEEN AGREED

BEFORE INITIATING HIGH-DOSE TREATMENT:

Exclude contra-indications:

- Perform ECG* - to establish a baseline, and exclude cardiac contraindications, including long QT syndromes.
- Check LFTs* – to exclude hepatic impairment

Consider other risk factors:

- Personal or family history of cardiac disease (MI, arrhythmia)
- Renal impairment
- Alcoholism / smoking
- Old age
- Obesity
- Interaction with concomitant medication, e.g. potential to cause QT-prolongation, electrolyte disturbance or CYP-enzyme inhibition)

Other baseline checks*:

- U&Es
- Pulse, supine and standing BP
- Temperature
- Prolactin
- Blood glucose
- Lipid profile
- Weight / BMI / waist circumference
- Cognitive function (especially in older people)

** Some patients may require PRN antipsychotics or rapid tranquilisation on admission which results in HDAT; if the patient is too unwell or refuses ECG/bloods/physical examination before such treatment is needed the decision to proceed with treatment should be recorded in the case notes.*

WHEN HIGH-DOSE TREATMENT INITIATED:

- Complete a "High Dose Antipsychotic Treatment Monitoring Sheet" and place with the drug prescription and administration record chart (for inpatients) or in the patient's notes (outpatients)
- Add an alert to Paris

AFTER HIGH-DOSE TREATMENT HAS COMMENCED:

- Where possible increase the dose of regular medication slowly, ideally over intervals of at least one week. Allow adequate time for response after each dose increment before a further increase is made
- Review progress at least once every 3 months (more frequently in early treatment), using an appropriate rating scale to assess symptoms (e.g. BPRS) and side-effects (e.g. LUNSERS, AIMS)
- Reduce the dose of regular medication to within the licensed range if no significant response is observed.
- Continued use of high dose treatment where there is no clinical response should be justified in the case notes and consultants should consider seeking a second opinion from a colleague. The review should be documented in the case notes.

Monitoring (to be recorded on the "High Dose Antipsychotic Treatment Monitoring Sheet" and on Paris):

- ECG – repeat once steady-state reached after each dose increase, then routinely every 6 months. Repeat at times of acute illness, when interacting drugs are introduced or if patient experiences symptoms that could be due to arrhythmias, e.g. syncope or fits. If an ECG is not performed the reason should be documented in the notes.
- LFTs, U&Es, temperature, pulse/BP – check once steady-state reached after each dose increase, then every 3 months
- Prolactin, blood glucose, lipid profile - check once steady-state reached after each dose increase, then every 12 months
- Assess for signs of dehydration (e.g. thirst/dry mouth, lethargy, low volume/concentrated urine) 1 week after each dose increase, then 3 monthly
- Weight / BMI / waist circumference – every 3 months

Avoid initiating other medication which increase risks associated with HDAT, i.e. diuretics, anti-arrhythmics, anti-hypertensives, tricyclic antidepressants and drugs which might prolong QT interval, or increase serum antipsychotic levels. If unavoidable, seek advice from the Pharmacy team before prescribing.

High Dose Antipsychotic Treatment: Responsibilities.

Consultant Responsibilities (delegated to junior doctors as appropriate)

- Exclude potential reasons for sub-optimal response to standard treatments
- Exclude all other evidence-based strategies; initiate HDAT, as a time-limited trial, only after these strategies have failed or considered inappropriate
- Involve the multi-disciplinary team, the patient and/or their family and/or their advocate in decisions about using HDAT
- Consider the possible contraindications to and risks of HDAT for the patient concerned
- Consider effects of gender and ethnicity on pharmacokinetics of antipsychotic medicines
- Place an alert on PARIS if HDAT is initiated
- Ensure monitoring of side-effects is completed in line with this guidance
- Assess the response to and the need to continue HDAT every 3 months (can be extended to 6 months in patients who have been on HDAT for longer than 12 months and are clinically stable)
- Re-assess and record patient capacity and consent to HDAT at each review
- Review HDAT initiated by junior doctors at out-of-hours admission on the next working day

Prescriber Responsibilities

- Document reason for high dose in case notes. Include the risks and benefits of the strategy, the aims and when the outcome will be assessed
- Complete a “High Dose Antipsychotic Treatment Monitoring Sheet” when treatment initiated
- Amend / update T2/T3 forms to cover above BNF maximum doses
- Inform nursing staff and members of the clinical team of high dose status
- Review and respond to any risk factors or abnormalities identified through monitoring
- Check and review “as required” (PRN) antipsychotic medication regularly, including any for rapid tranquilisation, with a view to reducing dose or stopping where possible.
- If HDAT has been initiated during an inpatient admission, ensure that GP and relevant community mental health teams are informed of HDAT status and all baseline/on treatment monitoring that has been completed on discharge.
- Ensure a system by which the ongoing monitoring and reviews will be conducted by agreement with the community mental health team and / or GP
- Level 3 non-medical prescribers may initiate HDAT in line with the Trust NMP Policy, and only following communication with a consultant which must be recorded in Paris.

Transfer of prescribing

- High dose antipsychotic treatment is off-label - GP’s should be informed on an individual basis if being requested to prescribe
- There may be situations when the GP may not wish to accept prescribing responsibility for an off-label use of a medicine, in which case the patient should continue to be seen by specialist services and continuity of prescribing will be retained in secondary care

Pharmacist Responsibilities (inpatient settings only):

- Identify patients on high dose antipsychotics or identify the potential for high dose treatment e.g. maximum regular dose and PRN prescribed
- Ensure a “High Dose Antipsychotic Treatment Monitoring Sheet” has been completed and is placed with the patient’s drug prescription and administration record
- Ensure T2/T3 forms have been amended / updated to cover >BNF max. doses
- Advise on % BNF maximum doses being prescribed
- Advise on any interacting medicines and mitigation of risk
- Indicate on patient’s current drug prescription chart that high dose monitoring chart in use
- Prompt medical staff if monitoring not completed
- Ensure nursing staff are aware of all patients receiving HDAT

Nursing Staff Responsibilities

- Complete or arrange monitoring checks as prompted by monitoring sheet, prescriber or pharmacist
- Check that monitoring sheet is being completed and bring to medical staff attention if checks have not been done

All staff - Ensure that high dose status is discussed at each review

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HIGH DOSE ANTIPSYCHOTIC TREATMENT MONITORING SHEET

Date HDAT commenced: ……

Patient name:	**D.O.B:**	**NHS Number:**
Consultant:		**Ward/CMHT:**
Reason for HDAT: (record in Paris)		**Medication alert on Paris?** Y / N

Risk Factors – please circle		
Cardiac History? **Y / N**	Hepatic impairment? **Y / N**	Obesity? **Y / N**
QTc interval:	Renal Impairment? **Y / N**	Heavy smoker? **Y / N**

ECG	Pre-R×	At steady state after each dose increase	Every 6 months	
Date due				
Date performed				
Result	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*
Annual checks	Pre-R×	Steady state after each dose increase	Every 12 months	
Date due				
Date checked				
Prolactin	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*	
Blood glucose	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*	
Lipids	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*	
HDAT Monitoring.	**Pre-R_x**	**Check once steady state reached after each dose increase then every three months**		
Date due				
Date checked				
For each drug specify: Drug Total daily dose % BNF max If regular or PRN				
TOTAL %				
Interacting drugs?	Y/N	Y/N	Y/N	Y/N
If Yes, specify drug and effect:				
Above sections completed by:				
U&Es	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*
LFTs	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*	Normal/Abnormal*
Temperature				
Pulse				
Blood Pressure				
Weight / BMI / waist circumference				
Assess for hydration				
Patient consent documented?	Y / N	Y / N	Y / N	Y / N
Review of HDAT documented	Y / N	Y / N	Y / N	Y / N
Doctor's Signature: Doctor's Name				
***Abnormal Result**	**Record actions in PARIS**			

Keep with patient's drug prescription and administration record card. (File in investigations in patient's case notes)
Do not photocopy. For further supplies contact Pharmacy: LRH 0191 4415775, RPH 01642 837680/838360 or WPH 01325 552105