

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, LUNBERS), should be standard practice so that there is ongoing consideration of the risk: benefit ratio for the patient. Rigorous physical health 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 the POMH ready reckoner [on the intranet](#) or [at the back of this document](#));

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 including those prescribed for rapid tranquilisation (PRN or once-only)]

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% If different, max. doses for the elderly are shown in brackets
Oral	
	mg per day
Amisulpride	1200
Aripiprazole	30
Asenapine	20
Cariprazine	6
Chlorpromazine	1000 (500)
Clozapine	900
Flupentixol	18
Haloperidol	20
Lurasidone	148
Olanzapine	20
Quetiapine (Mania & MR preparations)	800
Quetiapine (Schizophrenia/standard-release preparations)	750
Paliperidone	12
Risperidone	16 (4) ^a
Sulpiride	2400
Zuclopenthixol	150
Injections	
	mg per day
Aripiprazole	30
Haloperidol	20
Olanzapine	20
Zuclopenthixol acetate [“Acuphase”] ^b	75 (50) per day; 150 (100) per 48 hours Max. cumulative dose 400 mg per course; max. 4 injections
Depots / long-acting Injections	
Aripiprazole	400 mg per month
Flupentixol decanoate [“Depixol”]	400 mg per week
Haloperidol decanoate	75 mg per week
Olanzapine	150 mg per week
Paliperidone – monthly [“Xeplion”]	150 mg per month
Paliperidone – 3-monthly [“Trevicta”]	525 mg every 3 months
Paliperidone – 6 monthly [“Byanli”]	1000 mg every 6 months
Risperidone - fortnightly or monthly injection	25 mg per week
Zuclopenthixol decanoate [“Clopixol”]	600 mg per week
References: eBNF (accessed September 2023); Maudsley Prescribing Guidelines 14 th edition (2021)	

a. Maximum 2 mg/day for “short term treatment (up to 6 weeks) of persistent aggression in patients with moderate-severe Alzheimer’s disease”
b. Acuphase® should be included in HDAT calculations to determine if additional monitoring is required for 7 days following administration

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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 (or equivalent professional body of home country) 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 electronic clinical record, including the assessment of risks and benefits, the aims of treatment and plans for assessment of response and outcome.
- [Choice & Medication](#) offer patient information on HDAT to support shared decision making with patients and carers, available as a [handy fact sheet](#) and a [very easy read handy fact sheet](#).
- A decision by a doctor below ST4 or a non-medical prescriber to prescribe additional regular or "as required" antipsychotic treatment for a patient admitted out-of-hours, which results in HDAT, must be made following discussion with an ST4 doctor or above whenever possible; if this is not possible, the decision must be reviewed by an ST4 doctor or above (includes SAS doctors) by the end of the next working day.
- Where second generation long-acting injections are prescribed and the recommended dose interval is "monthly", this should be followed. A regular 28-day dose interval is not recommended; any dose interval shorter than 28 days is considered as HDAT and is therefore not suitable for shared care.

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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 (and physical assessment of hydration status)
- Pulse, supine and standing BP
- Temperature
- Prolactin
- HbA1c
- 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 electronic clinical record.

WHEN HIGH-DOSE TREATMENT INITIATED:

- Complete a “High Dose Antipsychotic Treatment Initiation & Monitoring Record” and place with the drug prescription and administration record chart (for inpatients) or in the patient’s physical notes (community)
- Add an alert to the patient’s electronic clinical record

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 patient’s electronic clinical record.

Monitoring (record on the “HDAT Initiation & Monitoring Record” and/or in the electronic clinical record):

- Hydration – be mindful of signs of dehydration (e.g. thirst/dry mouth, lethargy, low volume/concentrated urine) on a continuous basis
- ECG – repeat once steady-state reached after the 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 electronic clinical record.
- LFTs, U&Es, temperature, pulse/BP – every 3 months
- Weight / BMI / waist circumference – every 3 months
- Prolactin, HbA1c, lipid profile - every 12 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.

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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 the patient's electronic clinical record if HDAT is initiated
- Ensure monitoring of adverse 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 the electronic clinical record. Include the risks and benefits of the strategy, the aims and when the outcome will be assessed
- Complete a "HDAT Initiation & Monitoring Record" chart 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 (an ST4 doctor or above if out of hours) which must be recorded in the electronic clinical record.

Transfer of prescribing

- HDAT is off-label and considered not suitable for transfer to GPs; this includes HDAT resulting from a combination of antipsychotics even if the dose of the individual drugs is within their respective BNF maximum dose. It also includes antipsychotics being used to augment clozapine therapy, where the combined dose is HDAT, even though the GP would only be required to prescribe the augmenting antipsychotic (in these cases the augmenting drug should be prescribed on the clozapine prescription)
 - GPs should be kept informed of details of HDAT prescribed by the Trust for their own clinical records
- There may be cases when the GP is willing to accept responsibility to prescribe HDAT to facilitate patient care; in such cases, responsibilities should be agreed between the TEWV team and GP on an individual case basis.*

Pharmacist/Accredited Pharmacy Technician 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/rapid tranquilisation prescribed
- Ensure a "HDAT Initiation & Monitoring Record" 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 [N.B. max dose may be different in elderly patients]
- Advise on any interacting medicines and mitigation of risk
- Indicate on patient's current drug prescription chart that high dose monitoring record 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 record chart / prescriber / pharmacist / accredited pharmacy technician
- Check that monitoring record chart is being completed; bring to prescribers' attention if checks haven't been done

All staff - Ensure that HDAT status is discussed at each review

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HIGH DOSE ANTIPSYCHOTIC TREATMENT INITIATION & MONITORING RECORD

Patient name:		D.O.B:		NHS Number:	
Consultant:			Patient record ID:		
Ward/CMHT:			Care Co-ordinator:		
Date commenced:		Reason for HDAT: <small>(record in patient record)</small>		Medication alert on patient record? (✓) <input type="checkbox"/>	
Risk Factors (tick✓):	Cardiac history <small>(personal or family)</small>			Consent statement on patient record? (✓) <input type="checkbox"/>	
	Hepatic Impairment			Any Interacting drugs & effects? :	
	Obesity				
	Renal Impairment				
	Heavy Smoker				
First HDAT Prescription					
Drug Name:		Total daily dose:	% BNF max	Regular / PRN / Once only (i.e. RT):	
		Total % BNF max:			
Baseline (pre-HDAT) monitoring					
		Result:		Date completed:	Comments:
Temperature:					
ECG (record QT interval):					
Pulse:					
Blood Pressure: <small>(supine & standing)</small>		supine:	standing:		
Weight/BMI/waist circ.:		Weight:	BMI:	Waist:	
Assess hydration status:					<i>Be continuously mindful of signs of dehydration in patients on HDAT</i>
Prolactin:		Normal / abnormal*			* Record abnormal results in the electronic patient record
HbA1c:		Normal / abnormal*			
Lipid profile:		Normal / abnormal*			
U&Es:		Normal / abnormal*			
LFTs:		Normal / abnormal*			
Form Completed by:		Name:		Signature:	Date:

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Patient name:

NHS Number:

HIGH DOSE ANTIPSYCHOTIC TREATMENT - ONGOING MONITORING RECORD

HDAT Monitoring (every three months):				
Date due:				
Date checked:				
For each drug specify:				
Drug				
Total daily dose				
% BNF max				
If regular/PRN/once only				
TOTAL %:				
Interacting drugs?	Y/N	Y/N	Y/N	Y/N
If Yes, specify drug and effect:				
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 circ.:				
ECG (at steady state after increase to HDAT, then every 6 months; or if acute illness/new interacting drugs):				
Date due:				
Date performed:				
QT interval:				
Annual checks (every 12 months):				
Date due:				
Date checked:				
Prolactin:		Normal/Abnormal*		
HbA1c:		Normal/Abnormal*		
Lipids:		Normal/Abnormal*		
Patient consent documented?		Y / N		
Review of HDAT documented?		Y / N		
Doctor's Name & Signature:				

*Record abnormal results in the electronic patient record

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	mg per day
Oral	mg per day
Amisulpride	1200
Aripiprazole	30
Asenapine	20
Cariprazine	6
Chlorpromazine	1000 (500)
Clozapine	900
Flupentixol	18
Haloperidol	20
Lurasidone	148
Olanzapine	20
Quetiapine (Mania & MR preparations)	800
Quetiapine (Schizophrenia)	750
Paliperidone	12
Risperidone	16 (4)
Sulpiride	2400
Zuclophenthixol	150
Injections	mg per day
Aripiprazole	30
Haloperidol	20 (N.B. TEVV max recommended dose is 15 mg per day)
Olanzapine	20
Zuclophenthixol acetate ["Acuphase"]	150 (100) single dose/48 hours Max. cumulative dose 400mg per course; max. 4 injections
Depots/long-acting Injections	
Aripiprazole	400 mg per month
Flupentixol decanoate	400 mg per week
Haloperidol decanoate	75 mg per week
Olanzapine	150 mg per week
Paliperidone [Xeplion]	150 mg per month
Paliperidone [Trevicta]	525 mg every 3 months
Paliperidone (Byanli)	1000 mg every 6 months
Risperidone	25 mg per week
Zuclophenthixol decanoate	600 mg per week
Refs: eBNF & Maudsley Guidelines 14 th edition (2021)	

Keep with drug prescription and administration record (inpatients) or file in case notes (community patients)
Do not photocopy. For further supplies contact your local Trust Pharmacy team
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POMH Ready Reckoner

N.B. the same % of max dose does not necessarily equate to dose equivalence – e.g. oral aripiprazole 15 mg/day (50%) is not therapeutically equivalent to oral quetiapine 375 mg/day (50%). Seek pharmacy advice on therapeutic equivalence.

The POMH ANTIPSYCHOTIC DOSAGE READY RECKONER is available on the trust intranet. Screen shots of VERSION 10 are published on the intranet version of this document.

As per agreement with POMH, the ready reckoner cannot be reproduced on the website version of this document.

For TEWV the ready reckoner can be found on the intranet here

<https://intranet.tewv.nhs.uk/download.cfm?ver=12218>

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