GUIDELINES FOR THE USE OF HIGH DOSE ANTIPSYCHOTIC THERAPY (HDAT)

Document Reference	G376
Version Number	V1.03
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Date last reviewed, (this version)	January 2022
Date of Next Review	January 2025
Ratified by: **Date**	Drug and Therapeutics Group 27 January 2022

VALIDITY – Documents should be accessed via the Trust internet to ensure the current version is used.

CHANGE RECORD

Version	Date	Change details
V1.00	Sep 2013	*Major change in practice for check list to be kept with Medicines Administration Card. Additional updates to content and checklits and inclusion of additional resources from POMH.*
V1.01	06.03.15	*Requirement to print HDAT monitoring form in blue added, POMH ready rekoner version updated and calculation examples revised*
V1.02	Decv-18	*Reviewed with minor ammendments and formating*
V.1.03	Jan 2022	*Ammendments on Section 3.7, 3.8, and Apendix 3 to reflect changes in practice after introduction of ePMA.* *Replaced Ready Reckoner with version 9* *Approved at DTG 27 January 2022*

Contents

1. INTRODUCTION

This guideline is a revision of the Guideline G376 which aims to provide the framework for safe prescribing, monitoring and documentation of High Dose Antipsychotic Therapy (HDAT) within Humber Teaching NHS Foundation Trust (HTNFT).

The Consensus statement on high-dose antipsychotic medication (Royal College of Psychiatry Council Report CR138, May 2006 was updated to CR190 November 2015) which now defines high-dose antipsychotics use as:

"A total daily dose of a single antipsychotic which exceeds the upper limit stated in the summary of product characteristics (SPC) or BNF *with respect to the age of the patient and the indication being treated*, and a total daily dose of two or more antipsychotics which exceeds the summary of product characteristics or BNF maximum using the percentage method."[1]

An alternative calculation method based on chlorpromazine equivalents exists. Converting the dose of each drug into 'chlorpromazine equivalents' mg/day. This method is based on a combination of limited clinical evidence, expert consensus, and relative potency for dopamine D_2 receptors[2] (however: HDAT is likely to be affected by side-effects that are not mediated through D_2-receptor blockade e.g. hypotension via α-adrenergic antagonism or sedation via H_1 antagonism. There is no accepted table of chlorpromazine equivalents.

Psychiatrists have different understandings of equivalent doses in clinical practice. There is no identified method to convert second generation agents, calculated high doses bear little relation to SPC.

The method used within HTNFT to calculate cumulative antipsychotic doses, the BNF % calculation method, converts the dose of each drug into a percentage of the BNF maximum recommended dose for that drug and then adds these together to attain a total percentage of the BNF dose. A cumulative dose of more than 100% is a high dose (see Appendix 1). This method is simpler as the BNF maximum dose is clearly stated (except for Trifluoperazine) but also has limitations, the BNF % calculation method takes no account of the use of combined antipsychotics with contrasting mechanisms of action e.g. clozapine and amisulpride and possible pharmacodynamic and pharmacokinetic interactions may affect such combinations so they may not reflect a simple addition of percentages. Some combinations of antipsychotic drugs have a greater potential for side-effects for example for Flupentixol 400mg 1/52 PLUS chlorpromazine 1000mg od and Olanzapine 20mg od PLUS aripirazole 30mg od **Both** = 200% combined BNF % MAX, but the combinations are unlikely to be equally safe and tolerable.

BACKGROUND

Why do clinicians use HDAT?

- A relatively common reason given is poor response to standard treatment
- A recent UK study[3] showed that prior to receiving clozapine,
  - Over a third had received antipsychotic treatment above the maximum licensed dose
  - Over a third were prescribed antipsychotic polypharmacy

Patient factors precipitating HDAT

- Evidence[4] indicates factors include
  - Younger age
  - Longer duration of illness
  - History of violence and aggression
- Plausible reasons may include
  - Severity and symptom profile of the illness,
  - Level of medication adherence
  - Amount of carer support
  - Other psychosocial factors
- No evidence of clear relationship between dosage and ethnicity in UK studies[5]

Prescribers Factors Predicting HDAT

- Limited psychopharmacological knowledge and scepticism about prescribing algorithms[6]
- Most potent prescriber factor contributing to HDAT is the use of combined antipsychotics[7]
- More likely if the combination includes an antipsychotic prescribed on a pro re nata: as required basis [5].
- There are several clinical rationales for prescribing combined antipsychotics [1&8]
  - to enhance or speed up the therapeutic effect
  - managing challenging symptoms such as behavioural disturbance and aggression
  - targeting a particular symptom or symptom domain
  - to treat schizophrenia failing to respond to standard antipsychotic regimens
  - clozapine augmentation with a second antipsychotic
  - some evidence that adding aripiprazole to some antipsychotics can treat raised prolactin levels and metabolic dysregulation caused by the main antipsychotic[9]

- In most cases antipsychotic combinations are likely to increase the side-effect burden, compared with monotherapy
- Evidence from RCTs to support combinations is scarce[10]

Dose related side-effects

Most antipsychotic adverse effects may be dose-related, associated with increases in dose, the risk increasing with the speed of drug delivery or dosage increase, but some reactions are unpredictable, reflecting individual patient susceptibilities, (idiosyncratic reactions). Some reactions are neither clearly idiosyncratic nor dose-related. Several factors potentially confound dose–response relationships, including the pharmacokinetics of the drug, the role of metabolites, and clinical characteristics of the individual patient. [1]

EPS

It is well established that acute Extrapyramidal Side-effects (EPS) are more common with high-dose antipsychotic medication [11]. Generally, studies demonstrate that second-generation antipsychotic drugs induce fewer EPS than haloperidol, even at low doses, and that patients receiving the second-generation drugs consistently seem to be less likely to be prescribed anticholinergic drugs. Current evidence also generally supports a lower risk of tardive dyskinesia with second-generation antipsychotics compared with first-generation antipsychotics [12]

NMS

Neuroleptic malignant syndrome (NMS) is a rare but potentially life-threatening idiosyncratic reaction to certain psychiatric drugs, most commonly antipsychotics. The relationship between NMS and antipsychotic drug variables is uncertain. The syndrome is not clearly dose-dependent, but high dosage, rapid introduction, or escalation of the dosage, and use of intramuscular agents might all be risk factors [13].

Seizures

Antipsychotics lower the seizure threshold, individual agents are associated with different risk. Among the first-generation antipsychotics, the risk of seizures seems highest with chlorpromazine. Among the second generation antipsychotics, the risk of seizures is greatest with clozapine, again , higher doses and rapid dose increases enhance the risks as does the presence of pre-existing organic brain disease [1]

Cardiac adverse effects

A link between antipsychotics and ventricular arrhythmias and sudden death is well established, a consensus on event frequency is currently lacking [1]. Many antipsychotics prolong ventricular repolarisation, potentially giving rise to a prolonged QT interval on the ECG [14]and to a ventricular tachycardia termed *torsade de pointes* (TdP). TdP typically manifests as convulsions, dizziness and syncope, but it can also lead to ventricular fibrillation and sudden cardiac death. The QT interval is subject to a number of influences, including gender, age, time of day and heart rate, the “QTc” measure allows correction for heart rate.

Problems in reliably measuring QTc (especially when the heart rate is over 100 beats per minute, as can be found in patients receiving antipsychotic medication). However **QTc intervals longer than 500 ms are a major risk factor** for TdP**.** [1]

Antipsychotic risk factors

Most antipsychotic drugs are associated with a small but definite increase in the frequency of QTc prolongation, TdP and sudden cardiac death. These risks are heightened with higher doses and autonomic arousal, and other risk factors. Vigilance for these complications is required in all patients and investigation of patients with symptoms such as syncope is always warranted [1].

Other risk factors

- Other indicators of abnormal repolarisation include abnormalities of the T-wave or large U-waves.
- Duration of therapy: TdP most often occurs early in therapy.[1]

- Presence of electrolyte abnormalities, for example hypokalaemia, hypocalcaemia, or hypomagnesaemia.
- Presence of diuretics, probably due to electrolyte abnormalities.
- Existing cardiovascular or liver disease
- Malnourishment and alcohol dependence
- Co-prescription of other drugs with cardiac effects or pharmacokinetic interactions
- Gender: women have a longer QT interval on average than men[15], a disproportionate number of episodes of drug-induced TdP occur in women [16]
- Drugs of abuse and recreational substances, possibly ecstasy and cocaine and there is good evidence that methadone is associated with dose dependent QTc prolongation and TdP events. [17]

Routine ECG is a key part of quality medical care. For assessing cardiovascular risk a detailed family and personal history is also very valuable. CR 190 suggests an ECG prior to, and ECG monitoring during, antipsychotic therapy is **particularly** important in the following situations:

- High-risk antipsychotic drug treatment is contemplated (e.g. pimozide, haloperidol, sertindole
- High-dose or short-acting, parenteral antipsychotic drug therapy is to be used in an elderly patient or a patient with a history of cardiovascular disease.[1]

Urea and electrolytes should also be checked (**particularly plasma potassium**), especially in patients at higher risk of electrolyte abnormalities (e.g. patients with anorexia nervosa, liver disease, diuretic use, or dehydration).[1]

ECGs should be performed every few days following initiation of high dose treatment or during a period of dose escalation, until it is judged that steady state concentrations have been reached. Thereafter, ECG and electrolyte assessment is recommended every few months, at times of acute illness, when potentially interacting drugs are introduced or if the patient experiences symptoms that could be due to arrhythmia, for example syncope or fits [18]

Modifiable risk factors for ischaemic heart disease (e.g. smoking, hypertension, hyperlipidaemia, sedentary lifestyle) should be identified and managed appropriately.[1]

Summary
Doses above the BNF maximum are more likely to occur with the co-prescription of depot and oral medication or typical and atypical drugs. It should also be noted that the prescribing of ‘prn’ antipsychotics may contribute to high-dose neuroleptic use.
Potential side-effects of high-dose antipsychotic regimens should be monitored appropriately, by systematic enquiry, physical examination, ECG, and appropriate haematological investigations.[1]

- Cardiotoxicity- need to monitor
  - ECG
  - U & Es and LFTs (or BCP)
- Increased risk of physical side effects- monitor

    - Weight
    - BMI
    - Waist
    - BP (also consider postural hypotension)
    - Pulse
- Increased risk of metabolic disturbance- monitor
    - HbA1c
    - Prolactin (osteoporosis and fragility fractures risk)
    - Lipids
- Increased risk of seizures
- Increased risk of sedation

CR190 highlights there is currently little evidence for the efficacy of HDAT in any clinical setting, yet clear evidence exists for greater side effect burden and the requirement for appropriate safety monitoring within HDAT.[1]

Key recommendations of CR190:

- HDAT should be seen as an explicit, time-limited individual trial with a distinct treatment target
- HDAT should be reviewed at 3/12
- There should be a clear plan for regular clinical review including safety monitoring
- HDAT should only be continued if there is evidence of benefit that is not outweighed by tolerability or safety problems

All patients on high-dose antipsychotic treatment must be monitored. These guidelines provide information to clarify the identification of patients on high-dose antipsychotics, factors to be taken into account before such prescribing and the documentation required when antipsychotics are prescribed at high-dose.

The evidence to support combined antipsychotic prescribing is limited and outlined in the **POMH resource Combing Antipsychotics**.

(Double click to access and print out the full document)

POMH UK
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www.rcpsych.ac.uk/pomh

Combining Antipsychotics?

Why?	How good is the evidence that two antipsychotics are better than one?	
To manage acute behavioural disturbance (oral PRN)	Poor	Some studies show that some oral antipsychotics are effective in managing behavioural disturbance. See caveats under IM below.
To manage acute behavioural disturbance (IM 'RT')	Poor	NICE recommends IM olanzapine or haloperidol in patients whose behaviour is driven by psychosis. Trial evidence is in patients not receiving regular antipsychotics. A benzodiazepine alone may be as effective and safer.
To manage chronic behavioural disturbance	None	Some evidence supports the effectiveness of clozapine (monotherapy) in managing chronic aggression.
To manage relapse in a patient previously stabilised on a single antipsychotic	Poor	Studies have shown that increasing the dose of an established antipsychotic in a relapsed patient is no more effective than continuing the same dose. Combinations have not been systematically studied.
While switching from one drug to another	Limited	The dose of some antipsychotics (eg clozapine) needs to be increased slowly and cross titration is sensible. This should be complete in 4-6 weeks.
To speed up the onset of effect or enhance the size of the therapeutic effect	Poor	Response takes time. High initial doses do not speed up the onset of response. Combinations have not been studied. There is no evidence that combinations improve outcome.
To target different symptoms/symptom domain	Poor	Antipsychotics have differential effects on sleep but there is limited evidence to support clinically meaningful differences on core psychotic symptoms.
To reduce side effects	Poor	In most patients it is likely that side effects will be increased.
To allow administration by a different route	Uncertain	Very few antipsychotics are available in short acting IM, depot or orodispersible formulations. Reasonable attempts should be made to choose and use one route of administration. Combinations may be useful in some clinical circumstances.
Individual patient's/carer's choice	Limited	Choice is not real choice unless it is informed. If the patient can understand the potential benefits and risks of antipsychotic combinations and come to a reasoned decision, this should be supported.
Treatment resistance	Equivocal	Combinations involving clozapine should be considered before those involving other antipsychotic drugs.
Overall, there is a lack of evidence supporting benefit		

What do guidelines recommend?

1. **First line**; single (usually atypical) antipsychotic within the licensed dosage range for an adequate period of time.
2. **Second line**; different single antipsychotic within the licensed dosage range.
3. **Third line**; clozapine.
4. **Fourth line**; clozapine augmented with a second antipsychotic.
5. **Fifth line**; some guidelines recommend that other combinations should be considered at this point but highlight that this approach is only justified following lack of response to all strategies listed above.

What happens in practice?

- Prescribing surveys show that 10-20% of outpatients with schizophrenia and an average of 50% of inpatients are prescribed a combination of antipsychotic drugs.
- In a high proportion of cases, the second antipsychotic is PRN.
- PRN prescriptions result in many patients being potentially exposed to high doses of antipsychotics.
- These findings are consistent across different countries (UK, USA, throughout Europe) and have been consistent over time.

What are the potential problems?	How good is the evidence for this?
Difficulty determining cause and effect	Not knowing which antipsychotic has helped in the short term may lead to the patient receiving a higher than necessary dose (and more side effects) in the longer term.
Higher than necessary total dosage	There is no evidence that high doses of antipsychotics are more effective than standard doses. The major cause of high dose prescribing is combinations of antipsychotics.
Complex regime increasing the risk of non-adherence	In the general population, simple medication regimens involving a small number of tablets are more likely to be taken than complex regimens.
Increased cost	Some antipsychotics are expensive (£100-£200/month). Two cost more than one.
Increased side effects (acute or long term)	All antipsychotics have side effects. Profiles differ. One study shows that patients who receive combinations have 50% more side effects than those who receive 1 drug.
Drug interactions (pharmacokinetic and pharmacodynamic)	The safety of combinations of antipsychotics has not been studied systematically but there are many published case reports of serious side effects such as cardiac arrhythmias and neuroleptic malignant syndrome.
Increased duration of hospitalisation	One study found that the average length of hospital stay was more than 50% longer in patients who were prescribed combinations of antipsychotics.
?? Increased mortality	One study found that patients who were prescribed combinations were twice as likely to die over a 10 year period than those who took 1 antipsychotic.

More information and references can be found in the POMH-UK workbook; 'Making sense of combined antipsychotics'

2. SCOPE

This guideline is aimed at every qualified professional involved in the prescribing, administration and monitoring of HDAT within HTFNT

3. PROCEDURES

3.1. HDAT is identified using the resource available in Appendix 1

3.2. Before pursuing HDA, or on identification of HDAT, consider alternative approaches including adjuvant therapy and newer or atypical antipsychotics. Ensure that clozapine has been considered.

3.3. The responsibility to exceed the licensed dose of a single antipsychotic or a combination of more than one lies with the patient's Consultant Psychiatrist. The use of combinations from the same class should be avoided whenever possible. The decision should be discussed with the multidisciplinary team, the patient and/or carer if appropriate and valid consent obtained

3.4. For detained patients, ensure compliance with Part IV of the Mental Health Act for England 1983 specifically Section 58 which deals with the issues of consent in detained patients. The details of the decision-making process should be recorded in the patient's case notes including the clinical indication for use of HDAT. That the patient had been informed of the HDAT, or the reason why they have not been informed, should be documented in the notes.

3.5. HDAT may be prescribed in an emergency for acute symptoms. Ideally, this must be discussed with the Consultant Psychiatrist before it is prescribed: if it is not possible the reason should be documented, and the treatment reviewed at the next opportunity by the Consultant Psychiatrist or deputy. The indication for which any prn medication is prescribed should be clear and all prn medicines should be reviewed on a regular basis.

3.6. Only a Consultant Psychiatrist should make the decision to use regular HDAT. The decision should be documented in the patient's notes.

3.7. On identification of HDAT the patients Medicines Administration Record Card (MAR) should be annotated to indicate treatment with HDAT, this is to be annotated on ePMA, under Administration instructions box on the prescription window, to make staff administering aware of HDAT.

3.8. A High-Dose Antipsychotic Checklist (Appendix 3) should be completed for the patient in Lorenzo Clinical Charts, Medical tab, under the notes section.

3.9. While the patient is receiving HDAT the following factors should be taken into consideration to guide on appropriate dose and frequency of monitoring

- Cardiac history (particularly MI, arrhythmias, abnormal ECG)
- Hepatic / renal impairment
- Alcoholism / smoking
- Old age
- Obesity
- History of seizures
- Co-prescription of other medicines

3.10. Consideration should be given to the effect of potential drug interactions, specifically avoiding concomitant treatment with

- diuretics
- anti-arrhythmics
- anti-hypertensives
- tricyclic antidepressants
- medicines which might prolong QT interval
- medicines which may increase blood antipsychotic levels

3.11. A pre-HDAT ECG and biochemical profile should be obtained, if possible. If it is not possible and HDAT is to proceed, the decision to start must be adequately documented in the notes. Enquiry should be made regarding any family history of premature, sudden death.

3.12. If a prolonged QT interval is recorded (QTc > 440milliseconds), review treatment

- Consider cardiology assessment
- The reasons for continued treatment with HDAT in the presence of QTc prolongation must be recorded in the patient's case notes

3.13. Repeat ECG and biochemical monitoring, should be carried out a few days after treatment with HDAT is started (within 1 week)

3.14. Continued monitoring of ECG and biochemical profile should be carried out every 1-3 months in the early stages of HDAT

3.15. During long term HDAT, the frequency of ECG and biochemical profile monitoring should be established depending on clinical need

3.16. Additional physical monitoring should be carried out as outlined in HFT 'Guidelines for the medicines management of antipsychotics'. Modifiable risk factors for ischaemic heart disease (e.g. smoking, hypertension, hyperlipidaemia, sedentary lifestyle) should be identified and managed appropriately.

3.17. If high-dose antipsychotic therapy is being prescribed in the setting of Rapid Tranquillisation additional monitoring should be carried out as outlined in HFT 'Rapid Tranquilisation Guidelines'

3.18. During HDAT dose titration should ideally be carried out slowly at intervals of more than one week

3.19. During HDAT clinical improvement should be reviewed by the MDT at least every 3 months and dose reduction to within licensed limits made if clinical improvement is not adequate

3.20. Where clinical improvement is not adequate despite HDAT consideration should be given to seeking a second opinion

3.21. The Royal College of Psychiatrists Consensus Statement recommends monitoring of psychotic symptoms. Improvement in psychotic symptoms could be measured using a licensed, validated rating scale e.g. BPRS (Brief Psychiatric Rating Scale) and HoNOS (Health of the Nation Outcome Scales). Side effects could be monitored using a licensed, validated rating scale e.g. GASS (Glasgow Antipsychotics Side Effect Scale) or LUNSERS (Liverpool University Neuroleptic Side Effect Rating Scale). These should be performed at weeks 0, 6 and 12, then for each 3 monthly review

3.22. The use of and monitoring of HDAT should continue in secondary care until the effects of treatment on mental function and physical health have been established

3.23. GPs should be made aware of any patient who fulfil the definition of HDAT when returning to primary care prescribing

4. REFERENCES/DEFINITIONS

Royal College of Psychiatry. Consensus statement on high-dose antipsychotic medication. Council Report CR138, May 2006

Harrington et al (2002). The results of a multi-centre audit of the prescribing of antipsychotic drugs for in-patients in the UK. Psychiatric Bulletin, 26, 414-418

POMH- Combining Antipsychotics 2006

POMH Antipsychotic Dosage Ready Reckoner- Version 5 Feb 2015

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Appendix 1 - IDENTIFICATION OF PATIENTS ON HIGH-DOSE ANTIPSYCHOTIC MEDICATION

High dose antipsychotic prescribing may arise as a result of EITHER:

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

OR

B More than one antipsychotic prescribed concurrently where the sum of doses given expressed as a percentage of the BNF/ SPC maximum of each drug exceeds 100% (High-Dose through the prescribing of multiple drugs)

Examples

Regime Number 1	**BNF MAX**	**% BNF MAX**
Oral olanzapine 15mg daily	**= 20mg daily**	**75%**
Oral haloperidol 5mg up to tds	**= 20mg daily**	**75%**
Combined total %BNF max		**150%**

Regime Number 2	**BNF MAX**	**% BNF MAX**
Depot flupentixol 400mg every 2 weeks	**= 400mg every week**	**50%**
Oral olanzapine 5mg up to tds	**= 20mg daily**	**75%**
Combined total %BNF max		**125%**

Regime Number 3	**BNF MAX**	**% BNF MAX**
Oral quetiapine 600mg daily (immediate release for schizophrenia)	**= 750mg daily for schizophrenia** **= 800mg daily for mania** **=800mg m/r daily for schizophrenia**	**80%**
Oral haloperidol 5mg up to tds	**= 20mg daily**	**75%**
Combined total %BNF max		**155%**

Appendix 2 - POMH-UK Antipsychotic Dosage Ready Reckoner- Version 9

The combined maximum dose of antipsychotic as a percentage of BNF max can calculated using the POMH Antipsychotic Dosage Ready Reckoner- Version 4 below (double click to view fully)

ANTIPSYCHOTIC DOSAGE READY RECKONER - VERSION 9

February 2020 - *Always check you are using the latest version*

POMH-UK PRESCRIBING OBSERVATORY FOR MENTAL HEALTH-UK

Depot/long-acting injection and IM antipsychotics

Depot/LAI: dose calculated as mg/week

IM/Inhaled: dose in mg/day

Percentage of BNF maximum adult dosage

		5	10	15	20	25	30	33	40	45	50%	55	60	67	70	75	80	85	90	95	100%
Aripiprazole	Long-acting										50										100
Flupentixol	Depot	20	40	60		100					200					300					400
Haloperidol	Depot							25			37.5			50							75
Olanzapine	Long-acting										75										150
Paliperidone *	Long-acting													25							37.5
Paliperidone Trevicta**	Long-acting																				43.75
Risperidone	Long-acting										12.5					18.75					25
Zuclopenthixol	Depot			100	100			200			300			400			500	500			600
Aripiprazole	IM							10			15			20							30
Chlorpromazine	IM		25			50					100					150					200
Haloperidol	IM					5					10					15					20
Levomepromazine	IM		25			50					100					150					200
Olanzapine	IM					5					10					15					20
Zuclopenthixol acetate***	IM													50							75
Loxapine	Inhaled										9.1										18.2

* Maintenance dose licensed to be given monthly. ** Formulation licensed to be given every 3 months. *** A maximum of 150 mg in any 48-hour period and a maximum cumulative dose of 400 mg in any two week period.

To calculate a total daily prescribed antipsychotic dose as a percentage of the BNF maximum: determine the percentage of BNF maximum dosage for each antipsychotic that is prescribed, and then sum the percentages. For example, for a person prescribed clozapine 400mg a day and oral haloperidol 5mg PRN up to 3 times a day, the respective percentages would be 44% and 75%, giving a total antipsychotic prescribed dosage of 119% of the BNF maximum.

ANTIPSYCHOTIC DOSAGE READY RECKONER - VERSION 9

February 2020 - *Always check you are using the latest version*

POMH-UK PRESCRIBING OBSERVATORY FOR MENTAL HEALTH-UK

Oral antipsychotics

Dose in mg/day

Percentage of BNF maximum adult daily dosage

		5	10	15	20	25	30	33	40	45	50%	55	60	67	70	75	80	85	90	95	100%
Amisulpride	Oral							400			600			800			1000				1200
Aripiprazole	Oral							10			15			20							30
Asenapine	Oral					5					10					15					20
Benperidol	Oral							0.5			0.75			1							1.5
Cariprazine	Oral					1.5					3					4.5					6
Chlorpromazine	Oral		100	150			300				500		600			750					1000
Clozapine	Oral			150				300		400	450			600							900
Flupentixol	Oral			3				6			9			12				15			18
Haloperidol	Oral		2			5					10		12			15					20
Levomepromazine	Oral		100			250					500					750					1000
Lurasidone	Oral					37					74					111					148
Olanzapine	Oral					5		7.5			10					15					20
Paliperidone	Oral					3					6					9					12
Pericyazine	Oral					75		100			150			200							300
Pimozide	Oral		2		4		6		8		10		12								20
Promazine	Oral			150				300			400					600					800
Quetiapine*	Oral		75	100	150				300		375		450				600				750
Risperidone	Oral		2			4		6			8					12					16
Sulpiride	Oral			400				800			1200			1600			2000				2400
Trifluoperazine**	Oral		5		10		15		20		25		30		35		40		45		50
Zuclopenthixol	Oral		20		30			50						100							150

* 750mg/day max for schizophrenia, 800mg/day max for mania or if XL preparation used: % given for schizophrenia.
** No max dose stated in BNF or SPC; 50mg used by convention.

Appendix 3 - HIGH DOSE ANTIPSYCHOTIC THERAPY CHECKLIST

This form is available in Lorenzo clinical Charts under the medical tab, notes section, and must be completed for all patients prescribed high dose antipsychotic therapy prior to commencing treatment.

Patients Name: Gender:	NHS Number:
Date of Birth:	Consultant Psychiatrist:

High dose antipsychotic therapy checklist – *please circle as appropriate*

Has the patient failed to respond to two different classes of antipsychotic at maximum dosage for a suitable time period?	YES	NO

Past Medical History – cautions

Hepatic impairment?	YES	NO	Renal impairment?	YES	NO
Smoker?	YES	NO	Obesity?	YES	NO
History of cardiac disorders?	YES	NO	Impaired Glucose metabolism	YES	NO
Medicines with cardiac side-effects or interactions	YES	NO	History of serious substance dependence?	YES	NO

Details if YES:

Initial tests	Results	Date
ECG(QTc interval)		
Biochemical Profile		

Possible drug interactions

Tricyclic antidepressants	YES	NO	Other medication
Diuretics	YES	NO	

State reasons why high-dose therapy is to be initiated. If there are relative contra-indications outline risk management plan.

Consent to Treatment

Informal patient consenting to treatment ☐ Patient Signature:	Form T2 ☐	CTO11 ☐	Informal patient being treated under best interests ☐
Date:	Form T3 ☐ (or F39)	CTO12 ☐	

Authorisation of HDAT by Consultant

Signature:	Date:

Patients Name:	NHS Number:
Date of Birth:	Consultant Psychiatrist:

Antipsychotic Medication Details

Start Date	Medicine(s)	Dose and frequency	% BNF MAX	Stop Date

Total Cumulative % BNF Maximum

Current % BNF MAX							
Date							

Record of Retests- normal (N), abnormal (A) or refused (R)

Date	Test	Result			Test	Result			Note
	ECG	N	A	R	BCP	N	A	R	
	ECG	N	A	R	BCP	N	A	R	
	ECG	N	A	R	BCP	N	A	R	
	ECG	N	A	R	BCP	N	A	R	
	ECG	N	A	R	BCP	N	A	R	
	ECG	N	A	R	BCP	N	A	R	

Details of Abnormal Results- full details must be recorded in notes

Date	Test	Abnormality	Action