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High Dose Antipsychotic Therapy (HDAT) guideline

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Type of document	Guidance
Target audience	All CWP staff
Document purpose	To identify those patients receiving high dose antipsychotic therapy and provide details of monitoring requirements to ensure patient safety.

Approving meeting	Medicines Management Group	Date June 2017
Implementation date	July 2017	

CWP documents to be read in conjunction with	
MP1	Medicines Policy
MP10	Rapid tranquilisation policy

Document change history	
What is different?	Addition of appendix 4
Appendices / electronic forms	1. Addition of appendix 4 –POMH - UK antipsychotic dosage ready reckoner - version 6
What is the impact of change?	The updated document promotes the review and monitoring of HDAT in line with RCPsych guidance.

Training requirements	No - Training requirements for this policy are in accordance with the CWP Training Needs Analysis (TNA) with Learning and Development (L&D)

Document consultation - please note that the draft version of the updated policy was made available for comments on the intranet discussion board.	
East locality	Nina Geiger-Prescott (Clinical Pharmacist)
Wirral locality	Claire Dolan (Clinical Pharmacist)
West locality	Jennifer Southern (Senior Clinical Pharmacist), Julie Orton (Medicines Safety Officer)
Corporate services	None
External agencies	Mark Dickinson (Head of Prescribing and Medicines Optimisation for NHS Eastern Cheshire CCG, NHS South Cheshire CCG, and NHS Vale Royal CCG)

Financial resource implications	None

External references

1. Royal College of Psychiatry. Consensus statement on high-dose antipsychotic medication. Council Report CR190, November 2014
2. Harrington et al (2002a). The results of a multi-centre audit of the prescribing of antipsychotic drugs for in-patients in the UK. Psychiatric Bulletin, 26, 414-418
3. Mental Health Act 2007

4. Mental Capacity Act 2005
5. National Institute of Health and Clinical Excellence Clinical Guideline 178: Psychosis and schizophrenia in adults: prevention and management. Published date: February 2014
6. he Maudsley Prescribing Guidelines in Psychiatry; 12th edition; David Taylor, Carol Paton, Shitij Kapur; Wiley Blackwell 2015.

Equality Impact Assessment (EIA) - Initial assessment	**Yes/No**	**Comments**
Does this document affect one group less or more favourably than another on the basis of:		
- Race	No	
- Ethnic origins (including gypsies and travellers)	No	
- Nationality	No	
- Gender	No	
- Culture	No	
- Religion or belief	No	
- Sexual orientation including lesbian, gay and bisexual people	No	
- Age	No	
- Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
Is there any evidence that some groups are affected differently?	No	
If you have identified potential discrimination, are there any exceptions valid, legal and/or justifiable?		
N/A		
Is the impact of the document likely to be negative? - If so can the impact be avoided? - What alternatives are there to achieving the document without the impact? - Can we reduce the impact by taking different action?	No No N/A N/A	
Where an adverse or negative impact on equality group(s) has been identified during the initial screening process a full EIA assessment should be conducted. If you have identified a potential discriminatory impact of this procedural document, please refer it to the human resource department together with any suggestions as to the action required to avoid / reduce this impact. For advice in respect of answering the above questions, please contact the human resource department.		
Was a full impact assessment required?	No	
What is the level of impact?	Low	

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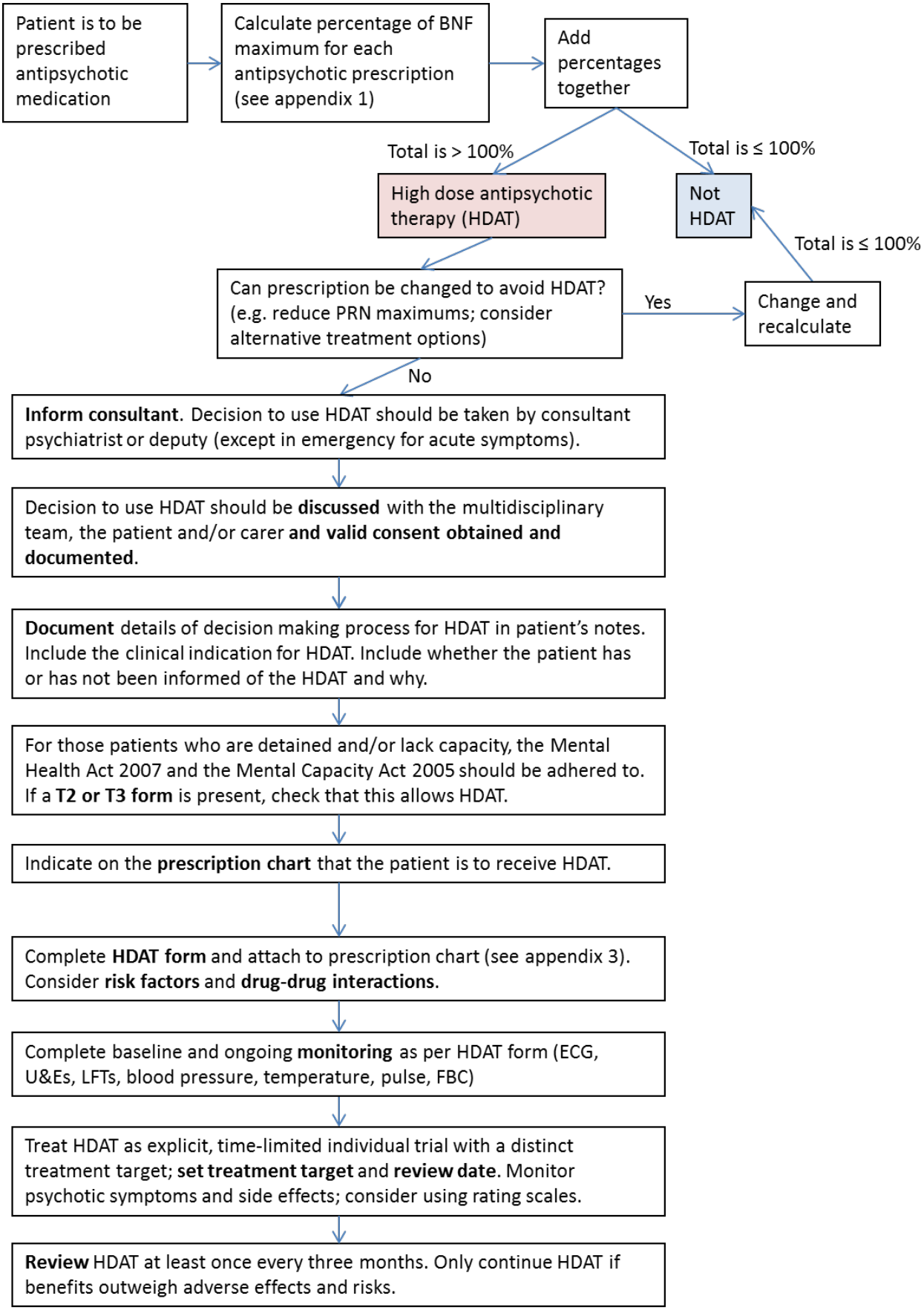
Quick reference flowchart – high dose antipsychotic therapy (HDAT)



1. Introduction

The Consensus statement on high-dose antipsychotic medication (Royal College of Psychiatry Council Report CR190, November 2014) defines high-dose antipsychotic use as:

"A total daily dose of a single antipsychotic which exceeds the upper limit stated in the SPC or BNF with respect to the age of the patient and the indication being treated, or a total daily dose of two or more antipsychotics which exceeds the SPC or BNF maximum using the percentage method."
NB: SPC = Summary of Product Characteristics; BNF = British National Formulary)

Doses above the BNF maximum are more likely to occur with the co-prescription of depot and oral medicine or typical and atypical antipsychotic medicines. It should also be noted that the prescribing of when required ('prn') antipsychotics may contribute to high-dose antipsychotic use.

All patients on high-dose antipsychotic treatment must be monitored. These guidelines attempt 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 in high-dose.

2. High Dose Antipsychotic Therapy (HDAT) Guideline

See appendix 1 for identification of patients on HDAT.

The Royal College of Psychiatric Consensus (CR190 November 2014) statement gives the following advice in relation to HDAT:

*"While there is **little convincing evidence that off-label prescribing of doses of antipsychotic medication above the licensed dosage range has any therapeutic advantage** in any clinical setting, there is clear evidence for a **greater side-effect burden** and the need for appropriate safety monitoring."*

*"The key recommendation is that any prescription of high-dose antipsychotic medication should be seen as an **explicit, time-limited individual trial** with a distinct treatment target."*

*"There should be a clear plan for regular clinical review including safety monitoring. The high-dose regimen **should only be continued if the trial shows evidence of benefit that is not outweighed** by tolerability or safety problems."*

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 decision should be discussed with the multidisciplinary team, the patient and/or carer and valid consent obtained. For those patients who are detained and/or lack capacity, the Mental Health Act 2007 and the Mental Capacity Act 2005 should be adhered to.

The details of the decision-making process should be recorded in the patient's case notes including:

- The clinical indication for use of HDAT;
- The patient has been informed of the HDAT, or the reason why they have not been informed.

HDAT may be prescribed in an emergency for acute symptoms. Ideally, this should be discussed with the consultant psychiatrist before it is prescribed. If it is not possible, then the reason should be documented and the treatment reviewed at the next opportunity by the consultant psychiatrist or nominated deputy.

Only the consultant psychiatrist or deputy should make the decision to use regular HDAT. The decision should be documented in the patient's notes.

Action:

- Indicate on the prescription chart that the patient is receiving HDAT:
  - Record the percentage of the BNF maximum next to each antipsychotic prescription.
  - Record the HDAT status on the front of the prescription chart in the special instructions box.
- The HDAT monitoring sheet (appendix 3) should be completed for the patient:
  - The HDAT monitoring sheet must be kept with the prescription chart.
  - A copy must also be filed in the patient's notes under investigations

(a) Consider risk factors such as:

- Cardiac history (particularly MI, arrhythmias, abnormal ECG);
- Hepatic / renal impairment;
- Alcohol use;
- Smoking;
- Old age;
- Obesity.

(b) Consider potential medicine interactions, specifically to avoid concomitant treatment with:

- Diuretics;
- Anti-arrhythmics;
- Anti-hypertensives;
- Tricyclic antidepressants;
- High dose methadone (>80mg / 24 hours);
- Medicines which might prolong QT interval, or increase blood antipsychotic levels.

(c) Obtain a pre-high-dose antipsychotic baseline ECG, if possible. If it is not possible and HDAT is to be prescribed anyway, the decision to start must be adequately documented in the notes. If a prolonged QT interval is recorded (QT_c > 440milliseconds), review treatment and consider cardiology assessment. If it is decided to continue treatment, record reasons for doing so in patient's case notes. Repeat the ECG:

- After a few days (within 1 week);
- After each dose increment;
- Every 1-3 months in the early stages of HDAT;
- Annually thereafter;
- Whenever clinically indicated (e.g. introduction or dose increase of a concomitant medicine that can prolong the QT interval; presence of other risk factors for QT interval prolongation).

(d) Serum urea and electrolytes and liver function should be checked before prescribing HDAT and after 1 month. Then every 3 months in the early stages of high dose treatment and thereafter as clinically indicated to ensure liver or renal failure are not developing.

(e) Monitoring of patients receiving antipsychotics should follow National Institute of Health and Clinical Excellence (NICE) Clinical Guideline 178: 'Psychosis and schizophrenia in adults: prevention and management', and include as a minimum, weight, lipids and glucose.

(f) If high-dose antipsychotic therapy is being prescribed in the setting of rapid tranquillisation or sedation then it is particularly important that the routine monitoring of a sedated patient is carried out, with particular attention to regular checks of pulse, blood pressure (BP), respiration, temperature and hydration. ECGs should be carried out frequently during dose escalation, if and when possible (see rapid tranquilisation policy).

Where possible increase the dose slowly ideally at intervals of at least one week.

Review clinical improvement at least once every 3 months, reducing the dose to within the licensed range if inadequate clinical improvement is observed, and consider an alternative antipsychotic. Consider clozapine for treatment-resistant schizophrenia as per NICE guidance. The review should be documented in the patients' notes.

Continued use of high-dose therapy where there is no clinical response should be justified in the case notes and consultants should consider seeking a second opinion.

The Royal College of Psychiatrists Consensus Statement recommends monitoring of psychotic symptoms. Consider the use of suitable rating scales for this purpose and for monitoring of side effects at appropriate intervals.

Improvement in psychotic symptoms could be measured using for example BPRS (Brief Psychiatric Rating Scale) and HoNOS, side effects could be monitored using for example LUNSERS (Liverpool University Neuroleptic Side Effect Rating Scale). These should be performed at weeks 0, 6 and 12, then for each 3 monthly review

The use of and monitoring of HDAT must continue in secondary care until and unless there has been agreement to transfer prescribing and monitoring responsibility to the patient's GP.

3. HDAT Monitoring: Duties and responsibilities within inpatient wards

3.1 Responsibilities of medical staff

- Record reason for high-dose in clinical notes;
- Complete the HDAT Monitoring Form;
- Inform patient and record consent in notes;
- Order ECGs, U&Es, and LFTs;
- Check HDAT is recorded on the T2 / T3 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 HDAT guideline is followed;
- If the patient refuses the recommended monitoring, then ensure that this is documented on the HDAT monitoring form and in the patient's notes;
- Ensure a system by which the required tests and reviews will be conducted is agreed with the relevant community mental health personnel and / or GP at discharge;
- **The decision to use high-dose antipsychotic therapy should only be taken by the Consultant Psychiatrist. A transfer of prescribing to a General Practitioner should be undertaken only after consultation and agreement with the General Practitioner.**

3.2 Responsibilities of nursing staff

- Temperature and BP check;
- Record "high dose" status in Nursing Notes;
- Check that monitoring sheet is being completed and bring to medical staff attention if checks have not been done;
- If the patient refuses the recommended monitoring, then ensure that this is documented on the HDAT monitoring form and in the patient's notes;
- Ensure that high-dose status is discussed at review.

3.3 Role of the pharmacist

- Identify that a patient is on HDAT within the usual clinical pharmacy arrangements;
- Promote the use of the HDAT Monitoring Form;
- Complete high-dose details and percentage of BNF maximum for each antipsychotic medicine;
- Complete interacting medicines section;
- Contact the prescriber and/ or consultant psychiatrist about the high-dose status.

4. Acknowledgements

- High Dose Antipsychotic Therapy Guidelines. Greater Glasgow and Clyde Health Board 2006;
- High Dose Antipsychotic Therapy Guideline, Pennine Care NHS Foundation Trust 2008.

Appendix 1 - Identification of patients on high-dose antipsychotic therapy

High dose antipsychotic prescribing may arise as a result of ***either***:

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

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 medicine exceeds 100% (High-Dose through the prescribing of multiple medicines).

For example:

- A patient on zuclopenthixol depot 300mg weekly and olanzapine 15mg daily;
- Sum of percentages: 50% + 75% = 125% (>100%, therefore high-dose).

Oral antipsychotics	**Maximum licensed (adult) daily oral doses i.e. 100% (mg/day unless otherwise stated)**
Amisulpride	1200
Aripiprazole*	30
Chlorpromazine	1000
Clozapine	900
Flupentixol	18
Fluphenazine	20
Haloperidol	20 (NB: IM [short-acting] max is 12mg/day)
Lurasidone*	148
Olanzapine	20
Paliperidone*	12
Pericyazine	300
Perphenazine	24
Pimozide**	20
Prochlorperazine	100
Promazine	800
Quetiapine (immediate-release)	750 (schizophrenia) or 800 (mania)
Quetiapine (modified-release)*	800
Risperidone	16
Sulpiride	2400
Trifluoperazine	Not stated, 45 suggested
Zuclopenthixol	150
Depots and long-acting antipsychotic injections	**Maximum licensed (adult) weekly IM doses (mg/week – but note that not all of these are suitable for weekly administration)**
Aripiprazole **depot***	Approx. 100 (400mg monthly)
Flupentixol decanoate **depot**	400
Fluphenazine decanoate **depot**	50
Haloperidol decanoate **depot**	75
Risperidone **long-acting injection***	25 (50mg per fortnight)
Olanzapine embonate **depot***	150 (300mg per fortnight)
Paliperidone palmitate **depot***	Approx. 37.5 (150mg monthly)
Zuclopenthixol **depot**	600

Use of “Discretionary” (PRN or “as required”) antipsychotic medicine should also be taken into account.

* Non-formulary (requires MMG approval) ** Subject to annual ECG irrespective of dosage.

Appendix 2 – High dose antipsychotic therapy (HDAT) monitoring form

This form **must** be completed for all HDAT patients – preferably prior to commencing treatment.

Name of patient	
Consultant Psychiatrist	
NHS Number	

Initial tests	**Results**	**Date**	**Initial tests**	**Results**	**Date**
BP			LFTs (✓if ok)		
Temperature			BMI		
Pulse			RBG / FBG (glucose)		
QTc interval			HbA1c		
U&Es (✓if ok)			Lipid profile (✓if ok)		

PMH – contraindications	**PMH - cautions**	
History of cardiac disorders? – Y / N	Heavy smoker	Y / N
Details:	Severe respiratory disease	Y / N
	Epilepsy / seizures	Y / N
	Blood dyscrasias	Y / N
	Myasthenia gravis	Y / N
	Susceptible to angle-closure glaucoma	Y / N

Possible medicine interactions	
QT interval prolonging medicines (e.g. tricyclic antidepressants, citalopram)	Y / N
Inhibitors of antipsychotic metabolism (e.g. fluoxetine, paroxetine)	Y / N
Inducers of antipsychotic metabolism (e.g. carbamazepine)	Y / N
Medicines that increase the risk of fluid and electrolyte disturbances (e.g. diuretics)	Y / N
Hypotensive / antihypertensive medicines (risk of additive hypotensive effect)	Y / N
Lithium (increased risk of EPSEs and neurotoxicity)	Y / N

Consent	**High dose therapy mentioned on T2 / T3?**
☐ T2 ☐ T3	☐ Yes ☐ No

Has the patient failed to respond to two different classes of antipsychotic at maximum dosage for a suitable time period?	☐ Yes	☐ No
Please state the reasons why high-dose therapy is to be initiated. If there are relative contra-indications please outline the risk management plan.		

Consultant signature		Print name	

High dose antipsychotic monitoring form

Test		No 1	No 2	No 3	No 4	No 5	No 6
ECG (QTc) (before treatment, within first week, every 1 to 3 months during early stages, then annually)	Date						
	Result						
Urea & Electrolytes (✓ if ok) (before treatment, at 1 month, at 3 months, and when indicated)	Date						
	Result						
BP (before treatment and as clinically indicated)	Date						
	Result						
Temperature (before treatment and as clinically indicated)	Date						
	Result						
Pulse (before treatment and as clinically indicated)	Date						
	Result						
Full blood count (before treatment and as clinically indicated)	Date						
	Result						
LFTs (before treatment, at 1 month, at 3 months, and when indicated)	Date						
	Result						

Abnormal results – Please provide details

Test / result	Date	Comment	Action

Appendix 3 - Possible audit criteria for clinical audit / medicines use evaluation of the guideline

Criterion statement	Standard	Exceptions
All patients who are prescribed high-dose antipsychotics are identified in the notes	100%	None
Each patient identified as being on high-dose antipsychotics has a completed high-dose antipsychotic monitoring form	100%	None
There is evidence that after initiation of high-dose antipsychotic therapy, there was a repeat ECG within 1 week and 1-3 monthly thereafter	100%	High-dose antipsychotic treatment discontinued. Reason(s) for not performing ECG documented in notes.
The ECG report can be examined for the presence/absence of: - Ischaemic Heart Disease - Left Ventricular Hypertrophy in addition to QT	100%	None
There is evidence that 'prn' antipsychotic medicine is under review	100%	None
The patients' notes contain details of the treatment plan incorporating high-dose antipsychotic treatment and a rationale for treatment	100%	None
There is evidence of ongoing monitoring of urea, U&Es and LFTs during high-dose antipsychotic treatment	100%	None

ANTIPSYCHOTIC DOSAGE READY RECKONER - VERSION 6

March 2015 - *Always check you are using the latest version*

Depot/long-acting injection and IM antipsychotics

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Depot: 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%
Flupentixol	Depot	20	40	60		100					200					300					400
Fluphenazine	Depot					12.5					25					37.5					50
Haloperidol	Depot							25			37.5			50							75
Pipotiazine	Depot					12.5					25					37.5					50
Zuclopenthixol	Depot			100				200			300			400			500				600
Aripiprazole	Long-acting										50										100
Olanzapine	Long-acting										75										150
Paliperidone [+]	Long-acting													25							37.5
Risperidone	Long-acting										12.5					18.75					25
Aripiprazole	IM							10			15			20							30
Haloperidol	IM					3					6						10				12
Chlorpromazine	IM		25			50					100					150					200
Levomepromazine	IM		25			50					100					150					200
Olanzapine	IM					5					10					15					20
Zuclopenthixol acetate [++]	IM													50							75
Loxapine	Inhaled										5										10

[+] Maintenance dose. [++] 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 6

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CCQI

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
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
Perphenazine	Oral		4								12			16							24
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.