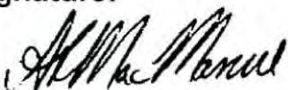
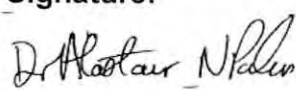
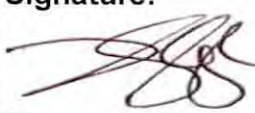


Guidance For Staff Working In Mental Health & Learning Disability Services For The Use Of High-Dose Antipsychotic Therapy (HDAT)

Co-ordinator: Principal Pharmacist, Mental Health and Learning Disability Services Chair, Mental Health Operational Medicines Management Group	Reviewer: Medical Director Mental Health and Learning Disability Services	Approver: Medicine Guidelines and Policies Group
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Signature: 	Signature: 	Signature: 
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Identifier: NHSG/HDAPsyc/ MGPG1272	Review Date: June 2025	Date Approved: June 2022
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Version 5

Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature:  _____

Title: Guidance For Staff Working In The Mental Health Service For The Use Of High-Dose Antipsychotic Therapy (HDAT)
Identifier: NHSG/HDAPsyc/MGPG1272
Replaces: NHSG/HDAPsyc/MGPG629, Version 4

Across NHS Boards	Organisation Wide	Directorate	Clinical Service	Sub Department Area
		Yes		

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Lead Author/ Co-ordinator: Principal Pharmacist, Mental Health and Learning Disability Services

Subject: Prescribing and prescription

Key word(s): Guidance, mental health, high dose, high-dose, antipsychotic medication, antipsychotics,

Document application: NHS Grampian – Mental Health Service

Purpose: To provide staff working in Mental Health & Learning Disability Services prescribing guidance for the use of high-dose antipsychotic therapy.

Responsibilities for implementation:

Organisational: Aberdeen City, Aberdeenshire and Moray IJB Management Teams

Hospital/Interface services: Medical Director Mental Health and Learning Disability Services and Associate Nurse Director, Grampian Mental Health and Learning Disabilities

Operational Management: Clinical Directors, Mental Health and Learning Disabilities and Aberdeen City HSCP, Aberdeenshire HSCP and Moray HSCP Service Managers

Unit: (Directorates) Clinical Leads

Departmental: Line managers

Area: Line managers

Hospital/Interface services: Assistant General Managers and Group Clinical Directors

Policy statement: It is the responsibility of supervisory staff at all levels to ensure that their staff are working to the most up to date and relevant policies, protocols procedures. By doing so, the quality of the services offered will be maintained, and the chances of staff making erroneous decisions which may affect patient, staff or visitor safety and comfort will be reduced.

Review: This policy will be reviewed at least every three years or sooner if current treatment recommendations change.

Responsible for review of this document: Mental Health Operational Medicines Management Group

Responsible for ensuring registration of this document on the NHS Grampian Information/ Document Silo: Pharmacy and Medicines Directorate

Physical location of the original of this document: Pharmacy and Medicines Directorate

Job/group title of those who have control over this document: Mental Health Operational Medicines Management Group

Responsible for disseminating document as per distribution list: Pharmacy and Medicines Directorate

Revision history

Date of change	Approval date of guidance that is being superseded	Summary of Changes (Descriptive summary of the changes made)	Changes Marked* (Identify page numbers and section heading)
November 2021	November 2018	<p>Headings added throughout.</p> <p>Background ‘There are several clinical rationales for prescribing combined antipsychotics including attempting to enhance or speed up therapeutic effect, managing behavioural disturbance and aggression or targeting a particular symptom such as affect instability.’ Removed.</p> <p>Pre-Treatment Checks Following added from Maudsley 2021: ‘Before prescribing HDAT ensure that:</p> <ul style="list-style-type: none"> • Sufficient time has been given to allow effect • At least two different antipsychotics have been tried sequentially • Clozapine has failed or not been tolerated • Medication adherence not in doubt • Adjunct medication with an antidepressant or mood stabiliser is not indicated • Psychological approaches have failed or are not appropriate’ 	<p>Page 1, paragraph 3</p> <p>Page 2</p>

		<p>High-Dose Antipsychotic Monitoring Link added to NHSG Responsibility for Prescribing across Secondary and Primary Care Appendix 1.</p> <p>References - updated.</p> <p>Consultation – Interface Group added.</p> <p>Appendix 1 - Additions For Aripiprazole: '15mg/day if given with strong CYP2D6 or CYP3A4 inhibitors 60mg/day if given with strong CYP3A4 inducers'. Link added to Summary of Product Characteristics (SPC).</p> <p>For Aripiprazole LAI: '300mg if given with strong CYP2D6 or CYP3A4 inhibitors 200mg if given with both strong inhibitors Avoid if strong CYP3A4 inducers'. Link added to SPC.</p> <p>'Cariprazine 6mg/day' added.</p> <p>For Lurasidone Link added to SPC.</p> <p>Appendix 2 'Pharmacist Responsibilities' changed to 'Specialist Pharmacist Responsibilities'. 'Medical Responsibilities' changed to 'Specialist Prescriber responsibilities for In-Patients and Out-Patients'. 'Nursing Responsibilities' changed to 'Nursing responsibilities for In-Patients'. Link to NHSG Responsibility for Prescribing across Secondary and Primary Care added.</p> <p>Bullet point 12 - wording revised and 'document the target symptoms, therapeutic response and side-effects ideally using validated rating scales' added.</p>	<p>Page 4, bullet point 4</p> <p>Page 4</p> <p>Page 4</p> <p>Page 5, Appendix 1</p> <p>Page 6</p>
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Guidance For Staff Working In The Mental Health Service For The Use Of High-Dose Antipsychotic Therapy (HDAT)

1. Background

For the purpose of this guidance high-dose is defined as a total daily dose of a single antipsychotic which exceeds the upper daily limit stated in the British National Formulary (BNF) or a total daily dose of two or more antipsychotics when expressed as a percentage of their respective maximum recommended doses and added together result in a cumulative dose of more than 100% (refer to [Appendix 1](#)).

There is no firm evidence that the use of high doses of antipsychotics is any more effective than standard doses. This holds true for the use of antipsychotics in rapid tranquillisation, management of acute psychotic episodes, persistent aggression and relapse prevention. However, there is clear evidence that the use of high doses of antipsychotics is associated with greater side-effect burden and the need for appropriate safety monitoring.

There is some evidence that the addition of aripiprazole to certain antipsychotics can treat raised prolactin and metabolic dysregulation caused by other antipsychotics. However, overall the evidence from randomised controlled trials to support the use of combined antipsychotics is scarce. Current evidence does not justify the routine use of high-dose antipsychotic medication in general adult mental health services, either with a single agent or combined antipsychotics. The use of high-dose antipsychotics should be an exceptional clinical practice and only ever employed when standard treatments, including clozapine, have failed or are not appropriate.

2. Initiation of High-Dose Antipsychotic Therapy

The decision to prescribe high-dose (of either an individual agent or through combination) should be taken explicitly and should be a time limited individual trial with a distinct treatment target. An individual risk-benefit assessment should be undertaken by a consultant psychiatrist in consultation with the wider clinical team, the patient and a patient advocate (if available, and if the patient wishes their presence). Clinical responsibility ultimately lies with the consultant psychiatrist. The patient's consent should be obtained and recorded in the clinical notes. If the patient refuses consent then the use of the Mental Health (Care and Treatment) (Scotland) Act 2003 will need to be considered. For patients detained under the Mental Health (Care and Treatment) (Scotland) Act 2003 with a treatment plan in place high-dose antipsychotic status must be mentioned on the T2B/T3B Form. If the patient is incapable of giving informed consent, use of the Adults with Incapacity (Scotland) Act 2000 may be required. Also consider any advanced statement the patient may have made.

3. Pre-Treatment Checks

Before prescribing high-dose antipsychotic therapy ensure that:

- Sufficient time (4 – 6 weeks at optimum dosage) has been given to allow previous treatment(s) to have effect
- At least two different antipsychotics have been tried sequentially
- Clozapine has failed, not been tolerated or wasn't appropriate
- Medication adherence not in doubt
- Adjunct medication with an antidepressant or mood stabiliser is not indicated
- Psychological approaches have failed or are not appropriate

Before initiation of and during treatment with, high-dose antipsychotic therapy consider any potential risk factors:

- Cardiac history (particularly MI, arrhythmias, abnormal ECG, lipids)
- Hepatic/renal impairment
- Alcoholism/smoking/substance misuse
- Aged over 65 years
- BMI <17.5 or >30
- Extreme physical exertion/stress or shock
- Metabolic disturbance (hypokalaemia, hypomagnesaemia, hypocalcaemia)
- Female gender.

Before initiation of and during treatment with, high-dose antipsychotic therapy consider any potential drug interactions, specifically aiming to avoid, where possible, concomitant treatment with:

- Drugs which alter electrolyte balance, e.g. diuretics
- Drugs which prolong QT interval, e.g. methadone, tricyclic antidepressants, anti-arrhythmics, certain antibiotics and antimalarial
- Drugs which can increase blood antipsychotic levels, e.g. inhibitors of Cytochrome P450 (fluoxetine).

NB: Refer to current individual Summary of Product Characteristics (SmPC), [BNF](#) and Maudsley Prescribing Guidelines for further information.

4. Review of High-Dose Antipsychotic Therapy

- There should be a clear plan for regular clinical review including safety monitoring. Ongoing assessment including documentation of target symptoms, response and side effects, ideally using validated rating scales, should be standard practice so that there is ongoing consideration of the risk-benefit ratio for the patient. Close physical monitoring including ECG is essential. High-dose antipsychotic therapy should only be continued if there is evidence of benefit that is not outweighed by tolerability or safety problems.

- Dose increases should be in relatively small increments allowing adequate time for response and this includes prescribing after the high-dose threshold has been passed.
- The use of additional “as required” medication should be kept under regular review and staff administering “as required” should be aware of its potential to raise the total daily dose of antipsychotic above the high-dose threshold.
- High-dose antipsychotic medication may be prescribed in an emergency for acute symptoms (refer to [NHS Grampian Staff Guidance for Rapid Tranquillisation for Use in the Adult In-patient Setting](#)). This should be discussed with the consultant or specialist registrar before it is prescribed.

5. High-Dose Antipsychotic Monitoring

- A High-Dose Antipsychotic Therapy Initial Monitoring Sheet ([Appendix 3](#)) should be initiated at start of treatment. Any risk factors, interacting medications, baseline and ongoing monitoring results must be recorded in the appropriate sections of the form. For professional responsibilities relating to high-dose antipsychotic monitoring see [Appendix 2](#).
- Before prescribing high-dose antipsychotics carry out an ECG to establish a baseline, and exclude cardiac contraindications, including a prolonged QT_c. If a prolonged QT interval is recorded (QT_c > 440ms for a male, QT_c > 460ms* for a female) review treatment, consider cardiology assessment. If the decision is taken to prescribe high-dose antipsychotic treatment, record reasons for doing so in patient’s case notes.
(*Recommended by Cardiology NHS Grampian)
- An ECG should be repeated:
 - When steady state serum levels are reached after every dosage increment and then every few months in the early stages of high dose treatment.
 - At times of acute illness.
 - When potentially interacting drugs are introduced.
 - If patient experiences symptoms that could be due to arrhythmia (e.g. syncope or fits).

Thereafter an ECG should be repeated every 6-12 months or more frequently if clinically indicated. Additional biochemical/ ECG monitoring is advised if drugs that are known to cause electrolyte disturbances or QTc prolongation are subsequently co-prescribed. If an ECG is not performed the reason should be documented in the patient’s clinical notes.

- Obtain baseline blood pressure, pulse, temperature, LFTs and U&Es. Repeat as clinically indicated or at least annually. In patients with cardiovascular disease or at high risk of electrolyte abnormalities, electrolyte assessment is recommended at least 3 monthly. In patients with risk factors for hepatic disease, e.g. a history of alcohol or drug misuse or established hepatic disease, repeat LFTs at least 3 monthly.

- The High-Dose Antipsychotic Therapy Initial Monitoring Sheet should be kept with the Prescription and Administration Record for in-patients and in the relevant section of the patient's psychiatric case notes for out-patients.
- Review progress at least once every 3 months, reducing dose to within the licensed range if no significant progress is observed and consider alternatives. Continued use of high-dose therapy should only be considered if benefits outweigh the risks. Consultants should consider seeking a second opinion from a colleague. The review should be documented in the patient's case notes.
- In addition to clinical assessment, measure improvement in psychotic symptoms and side effects using validated rating scales. It is suggested that these are performed at weeks 0, 6 and 12, then for each 3 monthly review.
- [Appendix 4](#) should be used for patients who continue on HDAT beyond 1 year.
- Prior to patients being discharged from hospital to the community, medical staff should discuss and agree with the General Practitioner who will be responsible for the ongoing monitoring and review and complete an individual patient care plan in line with [NHS Grampian Responsibility for Prescribing across Secondary and Primary Care Appendix 1](#).

6. References

1. The Royal College of Psychiatrists: Consensus on the use of High-Dose Antipsychotic Medication (Council Report 190) 2014
2. Taylor D et al: The Maudsley Prescribing Guidelines 14th Edition 2021, Wiley Blackwell
3. British National Formulary 82 September 2021 - March 2022

7. Consultation

Mental Health Operational Medicines Management Group Interface Group

Appendix 1: Identification Of Patients On High-Dose Antipsychotic Therapy

High-dose antipsychotic prescribing may be achieved in TWO ways:

1. Single antipsychotic drug prescribed at a daily dose above the BNF upper recommended limit (high dose single drug).
2. More than one antipsychotic prescribed concurrently that, when expressed as a percentage of their maximum recommended dosages and added together, result in a cumulative dose of >100%.

NB: In defining what constitutes a high-dose of antipsychotics for patients receiving more than one antipsychotic at doses within the normal BNF ranges, it is probably most satisfactory to add the percentages of the patient's current dose of antipsychotic expressed as a percentage of the recommended upper dose for each antipsychotic. Where this exceeds 100%, the patient is considered to be receiving a "high-dose". For example: a patient on zuclopenthixol depot 300mg weekly and olanzapine 15mg daily. Sum of percentages: 50% + 75% = 125% (>100%, therefore high-dose).

ANTIPSYCHOTIC NB: This list is not exhaustive, please refer to current BNF for complete list of antipsychotics available	MAXIMUM LICENCED ORAL (Adult) DAILY DOSE (100%) unless stated otherwise. NB: Maximum licensed dose may be lower in the elderly – refer to current BNF for individual drugs
Amisulpride	1200mg/day
Aripiprazole	30mg/day 30mg/day intramuscularly 15mg/day if given with strong CYP2D6 or CYP3A4 inhibitors 60mg/day if given with strong CYP3A4 inducers See SPC
Cariprazine	6mg/day
Chlorpromazine	1000mg/day 200mg/day intramuscularly
Clozapine	900mg/day
Flupentixol	18mg/day
Haloperidol	20mg/day 20mg/day intramuscularly
Levomepromazine	1000mg/day
Lurasidone	148mg/day 74mg/day if given with moderate CYP3A4 inhibitors See SPC
Olanzapine	20mg/day 20mg/day intramuscularly
Pimozide*	20mg/day

ANTIPSYCHOTIC NB: This list is not exhaustive, please refer to current BNF for complete list of antipsychotics available	MAXIMUM LICENCED ORAL (Adult) DAILY DOSE (100%) unless stated otherwise. NB: Maximum licensed dose may be lower in the elderly – refer to current BNF for individual drugs
Promazine	800mg/day
Quetiapine Immediate Release Quetiapine Sustained Release (XL)	750mg/day schizophrenia, 800 mg/day bipolar disorder 800mg/day schizophrenia and bipolar disorder
Risperidone	16mg/day
Sulpiride	2400mg/day
Trifluoperazine	Not stated by manufacturer (Suggest 30mg/day) ^[2]
Zuclopenthixol Zuclopenthixol Acetate	150mg/day 400mg total given intramuscularly in divided doses within a 14 day period
Aripiprazole Prolonged Release Injection	400mg monthly intramuscularly 300mg if given with strong CYP2D6 or CYP3A4 inhibitors 200mg if given with both strong inhibitors Avoid if strong CYP3A4 inducers See SPC
Flupentixol Decanoate Depot	400mg weekly intramuscularly
Haloperidol Decanoate Depot	300mg every 4 weeks intramuscularly
Paliperidone (Xeplion) Long Acting Injection	150mg monthly intramuscularly
Paliperidone (Trevicta) Long Acting Injection	525mg 3 monthly intramuscularly
Risperdal Consta Long Acting Injection	50mg every 2 weeks intramuscularly
Zuclopenthixol Decanoate Depot	600mg weekly intramuscularly

Pimozide* - Subject to special monitoring requirements irrespective of dose prescribed. Refer to BNF. Use of “discretionary” (“as required”) antipsychotic medication should also be taken into account.

Appendix 2: High-Dose Antipsychotic Monitoring: Responsibilities.

Specialist Pharmacist Responsibilities For In-Patients:

- Identify in-patients on high-dose antipsychotics and inform relevant consultant of high-dose status by letter.
- Complete form with the following information:
 - Patient details
 - High-dose details and %
 - Identify and document any co-prescribed medication, which could increase the risk of adverse effects.
- Attach “high-dose” label to Prescription and Administration Record.
- Audit use of high-dose antipsychotic medication.

Specialist Prescriber Responsibilities For In-Patients and Out-Patients:

- Ensure the ‘Guidelines for the use of High-Dose Antipsychotic Medication’ are followed for both in-patients and out-patients.
- Identify out-patients on high-dose antipsychotics.
- Document reason for high-dose antipsychotic medication in case notes.
- Inform patient and document consent in notes.
- Fill in Risk Factors on High-Dose Antipsychotic Monitoring Form.
- Order ECGs and review.
- Check U&Es.
- Check LFTs.
- For patients detained under the Mental Health (Care and Treatment) (Scotland) Act 2003 with a treatment plan in place ensure high-dose antipsychotic status is mentioned on T2B/T3B Form.
- For in-patients, on discharge or for out-patients, discuss and agree the high-dose antipsychotic monitoring plan with the GP and/ or other relevant community mental health personnel. See [Responsibility for Prescribing across Secondary and Primary Care Appendix 1](#) for an individual patient care plan.
- Check that monitoring sheet is being completed.
- Ensure high-dose status is regularly reviewed and document the target symptoms, therapeutic response and side-effects ideally using validated rating scales.

Nursing Staff Responsibilities For In-Patients

- Ensure all in-patients on high-dose antipsychotic therapy have this recorded on their nursing care plan.
- Ensure all patients on high-dose antipsychotic therapy have their blood pressure, pulse and temperature measured and recorded on NEWS 2 chart prior to commencing treatment.
- Ensure ongoing monitoring of blood pressure, pulse and temperature as per high-dose antipsychotic therapy monitoring guidance.
- Make comparison with previous recordings and report any abnormalities to medical staff.
- Record future ECG and blood test review dates for in-patients in the nursing care plan.

Appendix 3 - High-Dose Antipsychotic Therapy (HDAT) Initial Monitoring Sheet



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

NB: Both sides to be completed.

Patient name:	CHI Number:
Consultant:	Ward:

Risk Factors – please circle		
Cardiac History	Yes / No	Specify details:
Hepatic impairment	Yes / No	
Renal Impairment	Yes / No	
BMI <17.5 or >30	Yes / No	
Age >65 years	Yes / No	
Smoker	Yes / No	
Alcohol Misuse	Yes / No	
Substance Misuse	Yes / No	
Interacting Medication (If yes complete section below)	Yes / No	Doctor's Signature: Date:

High-Dose Antipsychotic Medication			Total combined % BNF Dose. Complete each time prescription amended	Signature and Date
Specify drug(s) and dose	Start date	Stop date		
Interacting medications? Y / N:			Clinical significance	Signature and Date
Specify:	Start date	Stop date		

Appendix 3 - High-Dose Antipsychotic Therapy Initial Monitoring Sheet (continued)

High-Dose Antipsychotic Monitoring. For abnormal results record actions / comments	Baseline	1 – 2 weeks	1 month	3 months	6 months	12 months
Date						
ECG (Record QTc interval)						
U&Es (✓ if OK)				(if req)	(if req)	
LFTs (✓ if OK)				(if req)	(if req)	
Blood Pressure, Pulse and Temperature	Record on separate monitoring sheet (NEWS 2 chart)					
Reason for HDAT documented in case notes? Y / N						
Consent obtained and documented? Y / N						
HDAT mentioned on form T2B / T3B? (Circle as appropriate)	N/A Yes/No			N/A Yes/No	N/A Yes/No	N/A Yes/No
HDAT reviewed (✓)						
Doctor's signature						

Date	Abnormal Result	Action/Comments	Doctor's Signature

MONITORING

- ECG – At baseline to exclude cardiac contraindications, including a prolonged QTc. Repeat when steady state serum levels reached after each dose increment and then every few months; at times of acute illness; when potentially interacting drugs are introduced; or if patient experiences symptoms that could be due to arrhythmia (e.g. syncope or fits). Thereafter an ECG should be repeated every 6-12 months or more frequently if clinically indicated. If an ECG is not performed the reason should be documented in the patient's clinical notes.
- Blood pressure, pulse and temperature at baseline and repeat regularly during titration.
- LFTs and U&Es at baseline and repeat as clinically indicated or at least annually. In patients with cardiovascular disease or at high risk of electrolyte abnormalities electrolyte assessment is recommended at least 3 monthly. In patients with risk factors for hepatic disease, e.g. a history of alcohol or drug misuse or established hepatic disease, repeat LFTs at least 3 monthly.

During hospital admission the high dose antipsychotic monitoring sheet should be filed in the patient's drug kardex/Prescription and Administration Record.

On discharge the high dose antipsychotic monitoring sheet should be filed in the appropriate section of the patient's notes.

Appendix 4 - High-Dose Antipsychotic Therapy (HDAT) Continuation Monitoring Sheet

To be completed for all high-dose therapy patients – preferably before commencing treatment.
NB: Both sides to be completed.

Patient name:	CHI Number:
Consultant:	Ward:

Risk Factors – please circle		
Cardiac History	Yes / No	Specify details:
Hepatic impairment	Yes / No	
Renal Impairment	Yes / No	
BMI <17.5 or >30	Yes / No	
Age >65 years	Yes / No	
Smoker	Yes / No	
Alcohol Misuse	Yes / No	
Substance Misuse	Yes / No	
Interacting Medication (If yes complete section below)	Yes / No	Doctor's Signature: Date:

High-Dose Antipsychotic Medication			Total combined % BNF Dose. Complete each time prescription amended	Signature and Date
Specify drug(s) and dose	Start date	Stop date		
Interacting medications? Y / N:			Clinical significance	Signature and Date
Specify:	Start date	Stop date		

Appendix 4 - High-Dose Antipsychotic Therapy (HDAT) Continuation Monitoring Sheet (continued)

High-Dose Antipsychotic Monitoring. For abnormal results record actions / comments	6 - 12 monthly (unless more frequently indicated – see below)					
Date						
ECG (Record QTc interval)						
U&Es (✓ if OK)						
LFTs (✓ if OK)						
Blood Pressure, Pulse and Temperature	Record on separate monitoring sheet (NEWS 2 chart)					
Reason for continuing HDAT documented in case notes? Y / N						
Consent obtained and documented? Y / N						
HDAT mentioned on form T2B/T3B? (Circle as appropriate)	N/A Yes / No	N/A Yes / No	N/A Yes / No	N/A Yes / No	N/A Yes / No	N/A Yes / No
HDAT reviewed (✓)						
Doctor's signature						

Date	Abnormal Result	Action/Comments	Doctor's Signature

MONITORING

- ECG - Repeat every 6-12 months or more frequently if clinically indicated. Additional biochemical/ECG monitoring is advised if drugs that are known to cause electrolyte disturbances or QTc prolongation are subsequently co-prescribed. If an ECG is not performed the reason should be documented in the patient's clinical notes.
- Blood pressure, pulse and temperature – Repeat regularly.
- LFTs and U&Es - Repeat as clinically indicated or at least annually. In patients with cardiovascular disease or at high risk of electrolyte abnormalities electrolyte assessment is recommended at least 3 monthly. In patients with risk factors for hepatic disease, e.g. a history of alcohol or drug misuse or established hepatic disease, repeat LFTs at least 3 monthly.

During hospital admission the high dose antipsychotic monitoring sheet should be filed in the patient's drug kardex / Prescription and Administration Record.

On discharge the high dose antipsychotic monitoring sheet should be filed in the appropriate section of the patient's notes.