East London NHS Foundation Trust

Policy for the use of high dose antipsychotic medication

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4.0	August 2011	Guidelines changed to “Policy” as per SUI recommendation
5.0	November 2012	Amendment to high dose monitoring tool. Amendment to Policy to reflect practice in community.
6.0	August 2014	Amendment to policy to reflect changes to BNF maximum doses for oral and intramuscular haloperidol. Amendment to high dose monitoring tool. Update of antipsychotic dosage reckoner.
7.0	August 2016	Amendment to high dose monitoring tool. Update of antipsychotic dosage reckoner
8.0	September 2020	Amendment to haloperidol IM maximum dose (from 12mg daily to 20mg daily), addition of aripiprazole LAI information Amendment to ECG monitoring frequency Comprehensive inclusion of monitoring requirements for those on HDAT Removal of paper-based HDAT monitoring form. Electronic RiO form (Psychotropic Medication Monitoring Form) to be used in its place. Amendment to pharmacist, junior doctor and nursing staff responsibilities Addition of appendix 1 – screenshot guide on how to complete the electronic RiO form for HDAT monitoring Addition of appendix 2 – HDAT Monitoring Summary table

Policy for the use of high-dose antipsychotic medication

1. Introduction

1.1 The purpose of this policy is to provide clear guidance on matters related to the use of high-dose antipsychotic medication in in-patients and community patients

1.2 ***The policy protects the right to treatment of patients who do require higher doses for effective treatment. For this, each patient should be assessed carefully by a fully trained psychiatrist.***

1.3 Unless otherwise stated, doses in the BNF are licensed doses – any higher dose is therefore **off-license**. The prescribing of licensed medicines outside the recommendations of the Marketing Authorisation alters (and probably increases) the doctor's professional responsibility.

1.4 The decision to raise the total dose of antipsychotics above the recommended upper limit must be taken by a Consultant Psychiatrist only.

1.5 As stated in the Trust Medicines Policy, nurses administering doses of antipsychotics above BNF maximum doses must check the case notes for the rationale behind this decision and confirmation of dose.

1.6 This document is made in conjunction with the 'Consensus statement on high-dose antipsychotic medication', from The Royal College of Psychiatrists, the November 2014 version[5]

1.7 Definition of High Dose Antipsychotic Therapy (HDAT)

1.7.1 Single antipsychotic drug prescribed at a total daily dose exceeding the recommended BNF upper limit/ the manufacturers Summary of Product Characteristic (SPC)

Or

1.7.2 More than one antipsychotic prescribed concurrently.

This is assessed by adding together the doses of each drug expressed as a percentage of their respective BNF maximum dose and where this exceeds 100%, the patient is considered to be receiving a "high-dose".

1.7.3 *For example*:

Zuclopenthixol depot 300mg weekly (50%) and Olanzapine 15mg daily (75%) = 50% + 75% = 125% (>100%, therefore 'high dose')

1.7.4 As required' antipsychotics contribute to HDAT.

For example

Olanzapine 20mg daily (100%) and haloperidol 5mg BD "as required" (50%) = 100% + 50% = 150%

Recommendations

Two or more antipsychotic drugs should only be given concurrently as part of a considered treatment plan.

- The use of more than one antipsychotic may cause increased adverse effects
- The use of more than one antipsychotic is associated with increased mortality
- The evidence-base supporting the use of more than one antipsychotic or higher than recommended maximum doses is poor.
- The benefit of using more than one antipsychotic must out weigh the risk of using high dose antipsychotic regimes
- The use of high dose antipsychotic therapy to be considered after several evidence based adequate trials of antipsychotic monotherapy including clozapine have failed[5]
- A trial of high dose antipsychotic therapy must be carefully monitored
- Supplementary prescribers should not take the decision to prescribe high dose antipsychotics

Guidelines for the Co-Prescription of Antipsychotics

1. Wherever possible one antipsychotic should be prescribed.

2. If no response is seen after 6 to 8 weeks at a therapeutic dose the antipsychotic should be switched to another antipsychotic. At this stage, it is imperative that compliance with the first drug has been checked thoroughly and verified.

3. Where no response is seen with the second antipsychotic, either consider switching to clozapine (as per NICE guidance) or to a third antipsychotic.

4. If there is no response or a lack of tolerance to the third antipsychotic or clozapine, consider adding in a second antipsychotic.

5. Before the second antipsychotic is prescribed, baseline Brief Psychiatric Rating Scale (BPRS) should be performed and the reason for co-prescription clearly documented in the notes.

6. A second BPRS should be performed 6-8 weeks after baseline and if there is no improvement in mental state, the withdrawal of the second drug should be considered.

2. The Policy

2.1 All treatment areas including In-patient, Community Mental Health Teams (CMHT's) and Specialist Services such as Early Intervention and Day Services must have a copy of the policy available. All staff that will be involved with high-dose antipsychotic medication must be confident to operate within the policy.

3. Alternatives strategies to high-doses of antipsychotics

3.1 Emergencies

3.1.1 In emergency, use rapid tranquilisation regime – see Trust Rapid Tranquilisation Guidelines for Adult, Older people or CAMHS.

3.2 Acute Treatment

3.2.1 In acute treatment, it is recommended that the dose of medication should be increased only gradually, e.g. weekly, so as not to exceed the dose needed to treat the psychosis. Any antipsychotic effects may take 1-2 weeks to become evident. Increasing the dose slowly is also thought to reduce the risk of neuroleptic malignant syndrome. If the patient is responding slowly and there is some urgency in the clinical situation, other methods of inducing a remission should also be considered.

3.3 When Required Medication

3.3.1 The use of PRN medication should be reviewed regularly and should include training for the clinical team on its use and alternative strategies. Staff should be aware of the potential for PRN medication to raise the total daily dose of antipsychotic above the high dose threshold.

3.4 Treatment Failure

3.4.1 For patients who have failed to respond to two antipsychotics at full dose, consider the following[1]:

3.4.2 Review the diagnosis. Consider organic causes, and illicit drug use.

3.4.3 Consider therapeutic drug levels, and compliance.

3.4.4 Has sufficient time been allowed for response to take place?

3.4.5 Consider reducing the antipsychotic dose slowly for a trial period. Some studies suggest a curvilinear dose response relationship, possibly because of inducing iatrogenic negative symptoms at very high dose. Rarely the anticholinergic effects of the antipsychotics may induce a toxic psychosis which will improve with dose reduction[3].

3.4.6 Consider adverse social and psychological factors which may be perpetuating the psychosis, including family factors, or if In-patient the ward environment and disturbances caused by other patients.

3.4.7 Consider specific psychological interventions aimed at target symptoms such as hallucinations or at improving the level of social role functioning, i.e. rehabilitation.

3.4.8 Consider other treatments such as mood stabilisers, or antidepressants, if there are severe mood symptoms, agitation or overexcitement.

3.4.9 Consider clozapine in treatment resistant patients i.e. those patients who have shown no or little response to at least two different antipsychotics.

Before combination antipsychotics are used, specific actions should be taken to ensure:

- The diagnosis is correct
- Treatment dose and duration has been adequate
- Plasma levels (if appropriate) are therapeutic and concordance with treatment ensured
- Alternative adjunctive drug therapies have been tried

Appropriate indications for use of more than one antipsychotic include:

- Rapid Tranquilisation (see trust rapid tranquilisation guidelines)
- Failed or partial response to clozapine
- Neutropenia or agranulocytosis with clozapine
- When switching from one antipsychotic to another (6 weeks crossover)
- As a temporary measure with depot medication during an acute exacerbation of illness

- **Inappropriate indications would include:**
- Failure to wait an adequate length of time for the first drug to have a full antipsychotic effect (6 months for clozapine, 6 weeks for all other oral antipsychotics and 8 weeks for depot medication)
- Where clinical improvement occurs before a switch of antipsychotics is completed
- Where patient is possibly treatment resistant and clozapine has not been tried
- Where benefit (as assessed by rating scales) does not outweigh the risk

4. Recommendations for high-dose antipsychotic prescribing

4.1 Discuss the reasons for the treatment, and consideration of alternatives, with the multidisciplinary team, and if possible the patient and their family or advocate.

4.2 Consider dose-related adverse reactions, and cumulative adverse reactions.

4.3 Obtain 'real or proper' consent where possible, and for detained patients ensure compliance with the provisions of part IV of the Mental Health Act 1983.

4.4 Consider a second opinion, or discuss with another consultant psychiatrist.

4.5 Rationale for using high dose antipsychotic therapy should be documented in the patient's notes on RiO.

4.6 Documentation indicating when a patient is receiving high dose antipsychotic therapy must be made on RiO. This should be recorded by completing the relevant sections for High Dose Antipsychotic monitoring on the Psychotropic Medication Monitoring form (see Appendix 1)

4.7 In-patient charts and community charts, where appropriate must indicate when a patient is receiving high dose antipsychotic therapy.

4.8 Increase the dose of antipsychotic(s) slowly.

4.9 Patient's progress should be reviewed at least 3 monthly and the dose reduced to within the licensed range if no significant progress is observed and alternatives considered.

4.10 Formal mental state examination eg. Brief Psychiatric Rating Scale (BPRS), should be performed at baseline, six and 12 weeks and then three monthly thereafter. If no clinical improvement is seen after six to eight weeks (change of at least 20% in BPRS score), consider reducing the dose.

4.11 Continued use of high dose therapy where there is no clinical response should be justified in the patient's medical notes.

4.12 A second medical opinion (formal for detained patients or in-house if informal) should be obtained for patients taking 'high dose' antipsychotics. It is the responsibility of the consultant to ensure all monitoring is done according to the policy. Community based patients should be monitored by consultant or by GP if there is an agreed shared care.

5. High risk patients and high-dose antipsychotic prescribing

5.1 Cardiac disorder, tobacco and alcohol use, obesity, illicit drug use, impaired glucose tolerance, diabetes, patients taking any drug which may lower the seizure threshold, hepatic or renal impairment and old age should be taken into consideration when starting a patient on high-dose antipsychotic medication.

6. Potential drug Interactions for high-dose antipsychotic prescribing

6.1 Consider potential Pharmacodynamic (additive) side effects as well as pharmacokinetic ones e.g. risperidone may inhibit the metabolism (and therefore increase levels) of certain antipsychotics and other psychotropic drugs.

6.2 Refer to current edition of BNF, or contact Medicines Information Centre, Pharmacy Department.

7. Mandatory monitoring for high-dose antipsychotic prescribing

7.1 ECGs are to be recorded at baseline where possible. Difficulties in obtaining a pre-treatment ECG in an acutely disturbed patient should not be underestimated and so, an ECG should be obtained 'at the earliest opportunity'.

Thereafter, an ECG should be obtained when steady state serum levels have been reached, after each dosage increment, and then every 6 – 12 months. Additional monitoring is advised for high risk patient (see 5.1), if drugs that are known to cause electrolyte disturbances or QTc prolongation are subsequently co-prescribed. If QTc is prolonged **(>440ms for men; >470msec for women)** or other adverse abnormality develops, treatment should be reviewed and cardiology assessment considered.

7.2 Monitor blood pressure, pulse, temperature weekly initially. Consider extending monitoring interval to yearly when treatment is stable or none of the listed risk factors present (refer to 5.1)

7.3 Monitor urea and electrolytes (including creatinine and eGFR) at baseline and then at a minimum of 3 monthly. Consider extending monitoring interval to yearly when treatment is stable or none of the listed risk factors present (refer to 5.1)

7.4 Complete Liver Function Tests (LFTs) at baseline, then yearly as part of routine physical health check.

7.5 Complete Full Blood Count (FBC) at baseline, then yearly as part of routine physical health check.

7.6 Monitor blood lipids (cholesterol; triglycerides) at baseline, at 3 months then yearly to detect antipsychotic-induced changes.

7.7 Monitor patient's weight (including waist size, and BMI, if possible) at baseline, frequently for 3 months then yearly.

7.8 Monitor plasma glucose (fasting sample, if possible) at baseline, at 4-6 months, then yearly. If levels are consistently elevated, obtain a HbA1c and refer to GP or specialist

7.9 Monitor prolactin at baseline, then at 6 months, then yearly.

7.10 Monitor Creatine Phosphokinase (CPK), a marker for NMS at baseline and then again if the patient is suspected to have NMS.

7.11 Monitor for side effects using either LUNSERS (Liverpool University Neuroleptic Side Effect Rating Scale or GASS (Glasgow Antipsychotic Side Effect Scale) for second generation antipsychotics.

7.12 Monitor patients for improvement in psychotic symptoms with BPRS or PANSS (Positive and Negative Symptom Score)

7.13 Refer to the High Dose Antipsychotic Therapy monitoring summary table (see appendix 2) for an overview of monitoring requirements.

7.14 **Community patients** – Continue monitoring at regular intervals, consider minimum once per year if patient maintained on stable dose of antipsychotic (see 4.12)

8. Resuscitation

8.1 All psychiatrists should have experience in resuscitation and know how to use the resuscitation equipment in the hospital. Each ward should have an appropriate procedure for dealing with cardiac arrest.
In the event of a cardiac arrest in community dial 999 and initiate basic life support. Click on link Resuscitation Policy

8.2 All sudden unexpected deaths which might be associated with antipsychotic prescribing should be reported using the yellow card scheme.

9. Antipsychotics – Dose Percentage Conversion Table

Oral Doses mg/day	**20%**	**25%**	**33%**	**40%**	**50%**	**67%**	**75%**	**80%**	**100%**
TYPICALS									
Benperidol			0.5mg		0.75mg	1mg			1.5mg
Chlorpromazine	200mg	250mg	330mg	400mg	500mg	660mg	750mg	800mg	1000mg
Flupenthixol			6mg		9mg	12mg			18mg
Haloperidol		5mg			10mg		15mg		20mg
Levopromazine	200mg	250mg			500mg		750mg		1000mg
Pericyazine		75mg	100mg		150mg	200mg			300mg
Promazine	160mg	200mg			400mg		600mg		800mg
Sulpiride	400mg	600mg	800mg		1200mg	1600mg	1800mg		2400mg
Trifluoperazine*	10mg			20mg	25mg				50mg
Zuclopenthixol	30mg		50mg	60mg	75mg	100mg			150mg
ATYPICALS	**20%**	**25%**	**33%**	**40%**	**50%**	**67%**	**75%**	**80%**	**100%**
Amisulpiride	240mg	300mg	400mg	480mg	600mg	800mg	900mg	960mg	1200mg
Aripiprazole			10mg		15mg	20mg			30mg
Asenapine		5mg			10mg		15mg		20mg
Clozapine	180mg	225mg	~300mg	360mg	450mg	600mg	675mg	720mg	900mg
Lurasidone		37mg			74mg		111mg		148mg
Olanzapine		5mg			10mg		15mg		20mg
Paliperidone		3mg			6mg		9mg		12mg
Quetiapine *(Schizophrenia)*	150mg				375mg				750mg
Quetiapine *(Mania)*		200mg			400mg		600mg		800mg
Risperidone		4mg			8mg		12mg		16mg
INTRAMUSCULAR INJECTIONS (I.M) mg/day	**20%**	**25%**	**33%**	**40%**	**50%**	**66%**	**75%**	**80%**	**100% Daily Dose**
Aripiprazole			10mg		15mg	20mg			30mg
Haloperidol		5mg			10mg		15mg		20mg
Loxapine (inhaled)					5mg				10mg
Olanzapine		5mg			10mg		15mg		20mg
Zuclopenthixol Acetate (Clopixol Acuphase)	**Maximum Cumulative Dose = 400mg in 2 week period Maximum 4 injections. Maximum of 150mg in 48 hours or 75mg in 24 hours**								75mg
DEPOTS/ LONG ACTING INJECTIONS (LA) mg/week	**20%**	**25%**	**33%**	**40%**	**50%**	**67%**	**75%**	**80%**	**100% Weekly Dose**
Flupenthixol Decanoate	80mg	100mg			200mg		300mg		400mg
Fluphenazine Decanoate**		12.5mg			25mg		37.5mg		50mg
Haloperidol decanoate			25mg		37.5mg	50mg			75mg
Olanzapine Embonate (LA)					75mg				150mg

Paliperidone palmitate						**25mg**			**37.5mg**
Pipotiazine Palmitate		**12.5mg**			**25mg**		**37.5mg**		**50mg**
Risperidone consta (LA)					**12.5mg**		**18.75mg**		**25mg**
Zuclopenthixol Decanoate		**150mg**	**200mg**		**300mg**	**400mg**	**450mg**		**600mg**
Aripiprazole Abilify Maintena									**100mg**

* There is no maximum dose for trifluoperazine stated in BNF/SPC; 50mg is used by convention

**The manufacturer of fluphenazine decanoate (Modecate®) injection had written to healthcare professionals advising that this product was to be discontinued by the end of 2018.

Table adapted from POMH-UK "*Antipsychotic Dosage Reckoner version 6: Mar 2015*

10. Responsibilities

10.1 Pharmacist Responsibilities

- Identify that a patient is on high-dose antipsychotics
- Inform the medical team, consultant, named nurse and care co-ordinator when their patient is prescribed HDAT and the percentage (%) it is prescribed above the BNF max
- Prompt the medical team to complete the Psychotropic Medication Monitoring Form (see appendix 1)
- Check that the Psychotropic Medication Monitoring Form on RiO is being updated and highlight any outstanding monitoring to the medical team, consultant and nursing team.
- Identify potential drug interactions, inform the medical team and record this on RiO and the discharge notification (if patient discharged on HDAT)

10.2 Junior Doctor Responsibilities

- Identify risk factors (see 5.1)
- Order ECGs
- Check U&Es
- Check LFTs
- Check blood lipids
- Check plasma glucose/HbA1c
- Check prolactin
- Check Creatine Phosphokinase (CPK)
- Record ECG, U&Es and LFTs, plasma lipids, plasma glucose/HbA1c monitoring results on RiO (Physical Health > Investigations Form)
- Document prolactin and CPK results by making a RiO entry
- Document BPRS scores
- Assess and monitor for side effects associated with HDAT
- Document reason for high-dose in case notes
- Inform patient and document consent in notes
- Complete the Psychotropic Medication Monitoring Form and relevant sections pertaining to HDAT on RiO (see appendix 1)
- Check high dose antipsychotic therapy (HDAT) is mentioned on consent to treatment or second opinion 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 a system by which the required tests and reviews will be conducted and is agreed with the relevant community mental health personnel & / or GP.

10.3 Nursing Staff Responsibilities

- Temperature check
- Blood pressure check
- Weight/BMI check
- Record temperature, blood pressure and weight/BMI on RiO (Physical Health > Observations and Measurements)
- Document “high dose” status in the nursing care plan and daily progress notes.
- Check that the Psychotropic Medication Monitoring form and the relevant sections pertaining to HDAT on RiO (see appendix 1) are complete
- Ensure that high-dose status is discussed at review
- Monitor for side effects associated with HDAT and report to the medical team

10.4 Consultant Responsibilities

- Ensure policy is followed for HDAT
- Monitor Community based patients as per policy
- Use of high-dose antipsychotic therapy is solely the responsibility of the consultant.

10.5 Non-Medical Prescribers (NMP)

- Non-Medical Prescribers should not make the decision to proceed with the use of high dose medication.
- Use of high-dose antipsychotic therapy is solely the responsibility of the consultant

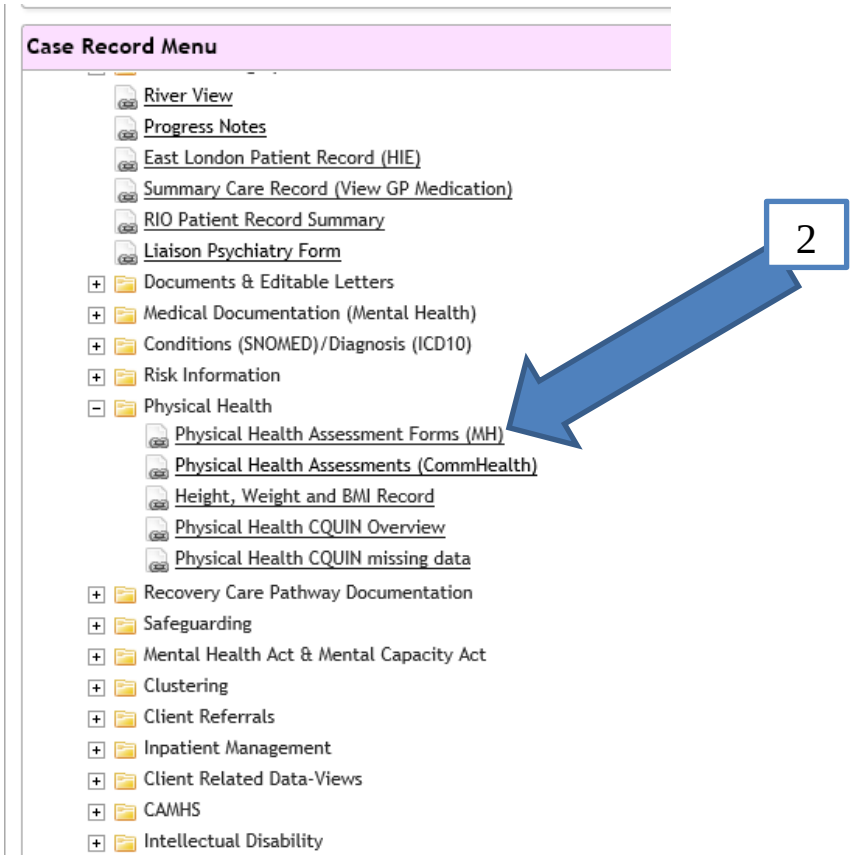
References

1. *Royal College of Psychiatrists Consensus statement on the Use of High Dose Antipsychotic Medication, Council Report CR190 November 2014*
2. *Summary Product Characteristic (SPC)for Haldol®. www.emc.medicines.org.uk. Accessed 9/08/2016.*
3. *Barnes. T and The Schizophrenia Consensus Group of the British Association for Psychopharmacology (2011). Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology. J Psychopharm 0 (0) 1-5.*
4. *Baldessarini RJ, Cohen BM, Teicher MH (1988)Significance of neuroleptic dose and plasma level in the pharmacological treatment of psychosis, Arch Gen Psych, 45, 79-90.*
5. *Central and North West London NHS Foundation Trust(For Adults), 2009, High Dose Antipsychotic Policy.*
6. *Bradford District Care NHS Trust, Guidelines for the Use of High Dose Antipsychotic Medication, May 2009.*
7. *Birmingham and Solihull Mental Health NHS Foundation Trust, Clinical Guideline: The Prescribing of High Dose and combination Antipsychotic Medication, Sep 2010*
8. ***POMH-UK** “Antipsychotic Dosage Reckoner version 6 Mar 2015.*
9. *www.bnf.org accessed 9/08/2016.*
10. Taylor D, Paton C, Kapur S: Maudsley Prescribing Guidelines in Psychiatry 12th Edition, 2015, WILEY Blackwell.

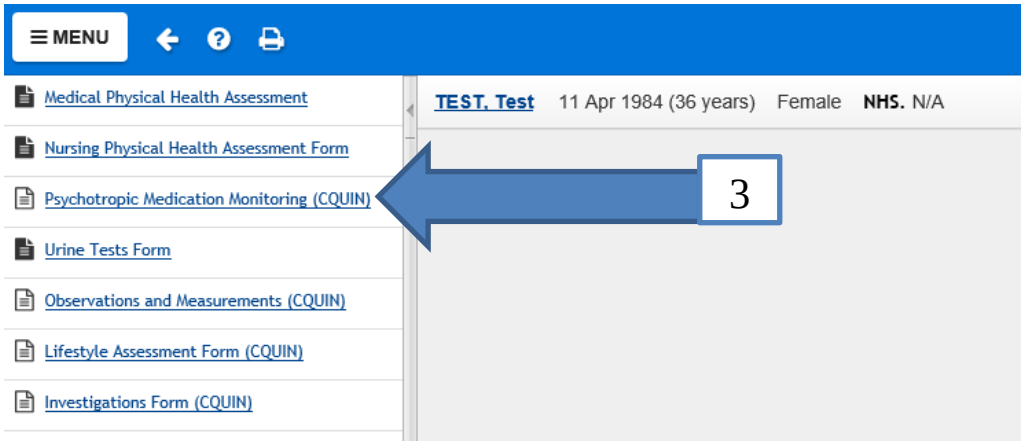
Appendix 1 **Psychotropic Medication Monitoring Form (electronic HDAT Monitoring form)**

Please see instructions below on how to access and complete this form. The completion of this form helps ensure all monitoring associated HDAT is recorded and easily accessible.

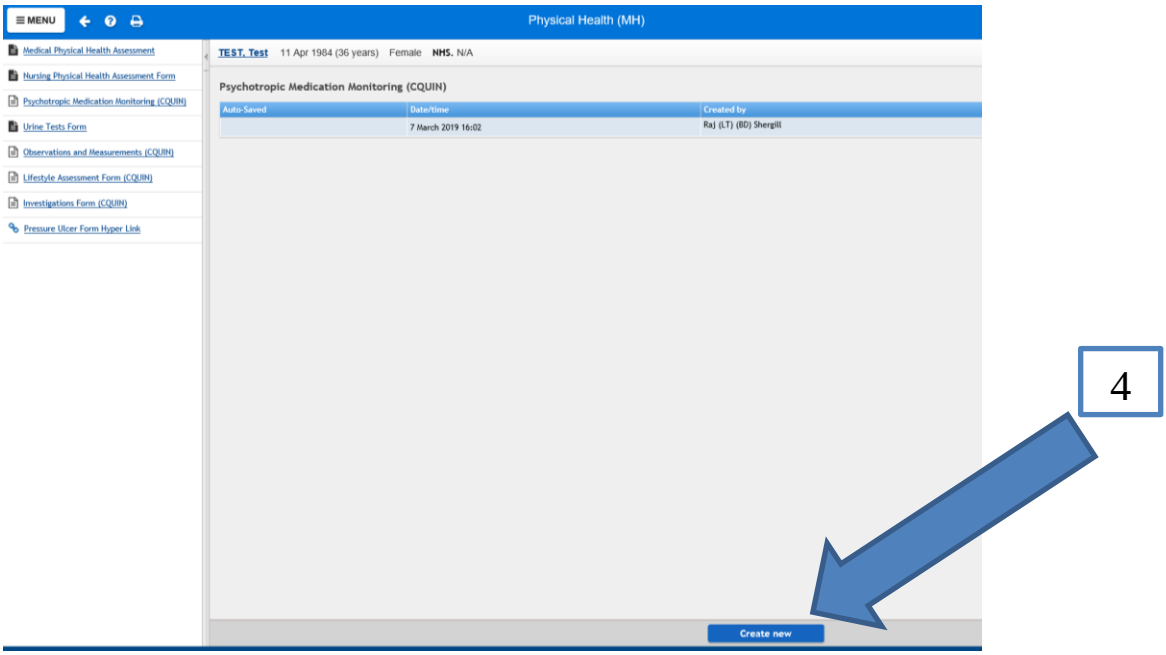
1. Access patient records on RiO
2. Open ‘Physical Health’ folder under ‘Case Record Menu’ and select ‘Physical Health Assessment Forms (MH)



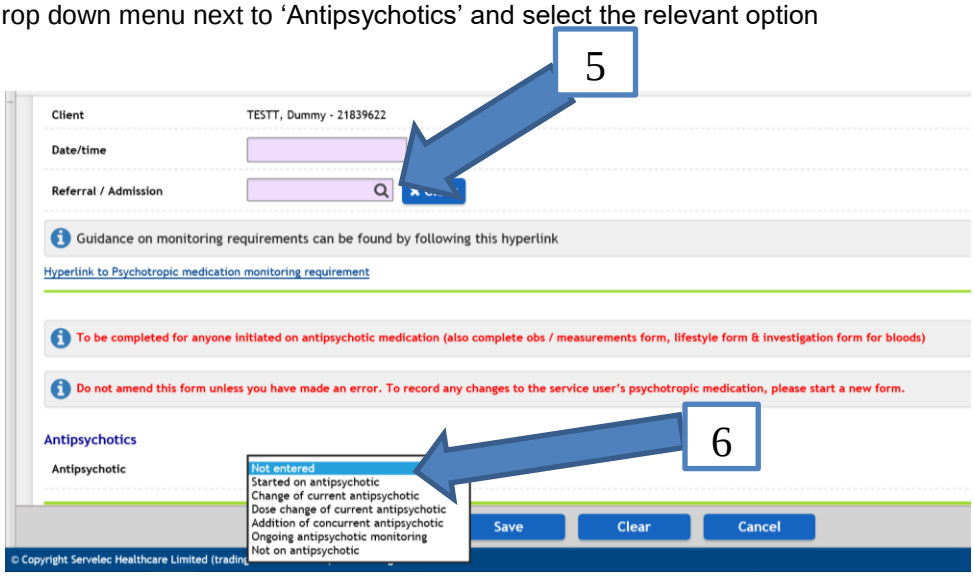
3. Select ‘Pscyhotropic Medication Monitoring (CQUIN)’



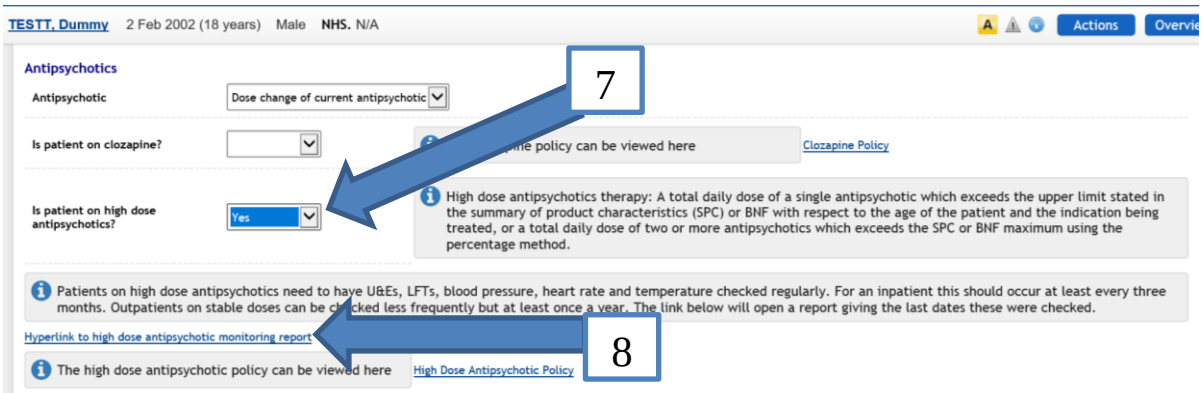
4. Select the ‘Create new’ tab



5. Populate the date/time
6. Select the drop down menu next to ‘Antipsychotics’ and select the relevant option

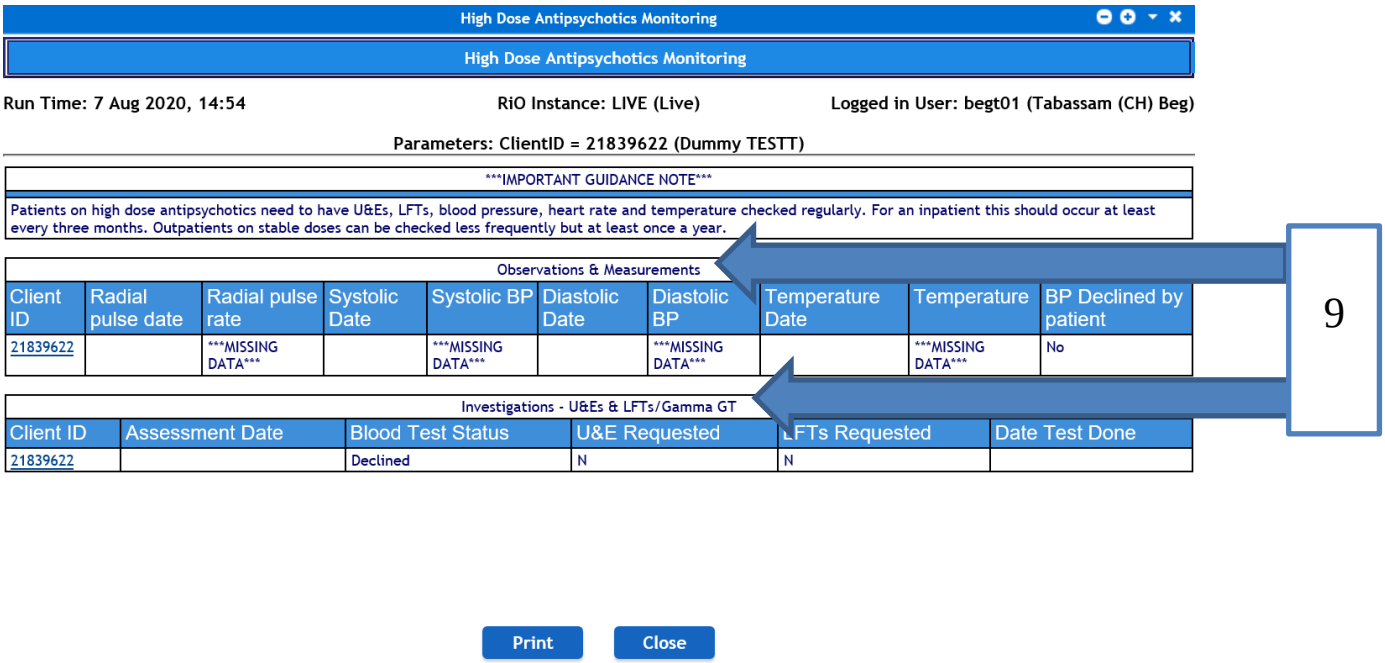


7. Select ‘Yes’ from the drop down menu next to ‘Is patient on high dose antipsychotics?’
8. You can view the status of each monitoring parameter by selecting ‘Hyperlink to high dose antipsychotic monitoring report’

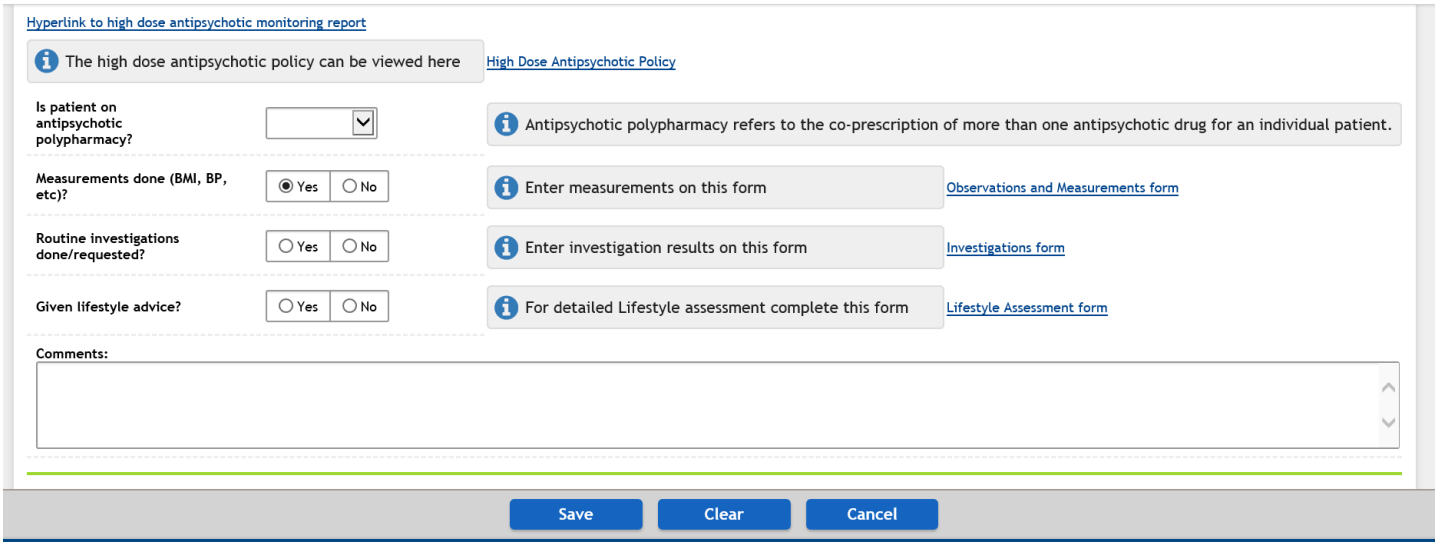


9. Once you have clicked on the hyperlink, a box will appear indicating the date each monitoring parameter had been recorded under ‘Observations & Measurements’ and ‘Investigations – U&Es & LFTs/Gamma GT’. After viewing, you can close this box.

Please note: ECG, Blood Lipids (cholesterol triglycerides), BMI, HbA1c Prolactin and Creatine phosphokinase (CPK) does not currently appear in this report box. Please see section 10 for who is responsible for recording each monitoring parameter and where.



10. To complete the form, answer the remaining questions. You can input results by clicking on the hyperlinks to the relevant forms and completing by the 'create new' function.
11. Save your form. You can then edit and view the form by repeating steps 1-3 and then accessing the form.



Appendix 2 **High Dose Antipsychotic Monitoring Summary table**

Test	Baseline	After each dose increase	Weekly initially	6 weeks	Min. 3 monthly during initiation phase	6 months	Annually
ECG*	✓	✓				✓	✓
Blood pressure	✓		✓				✓
Pulse	✓		✓				✓
Temperature	✓		✓				✓
U&Es (including creatinine or eGFR)	✓						✓
LFTs	✓						✓
FBC	✓						✓
Blood Lipids (cholesterol triglycerides) fasting sample if possible	✓				✓		✓
Weight (including waist size and BMI, if possible)	✓				✓		✓
Plasma glucose – fasting sample if possible- HbA1c	✓					✓	✓
Prolactin	✓					✓	✓
Creatine phosphokinase (CPK)** (marker for NMS)	✓						
Formal mental state exam e.g. BPRS	✓			✓	✓		

** All patients on high doses should have regular ECGs (baseline, when steady state serum levels have been reached after each dosage increment, and then every 6 – 12 months) Additional monitoring is advised if drugs that are known to cause electrolyte disturbances or QTc prolongation are subsequently co-prescribed. **monitor at baseline then if NMS suspect*