Mersey Care NHS
NHS Foundation Trust

MERSEY CARE NHS TRUST – HOW WE MANAGE MEDICINES

MM11 - High-Dose Antipsychotic Use Guidelines (local guideline)

Medicines Management Services aim to ensure that
(i) Service users receive their medicines at times that they need them and in a safe way.
(ii) Information on medicines is available to staff, service users and their carers

KEY ISSUES

Prescribing, administration and monitoring information for doctors, nurses and pharmacists involved in care of service users on wards and outpatient clinics of Mersey Care Trust who are receiving high-dose antipsychotic therapy to ensure the safest and most effective clinical practice.

Medicines Management Procedure – MM11
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1 DEFINITION

According to the consensus statement on high-dose antipsychotic medication by the Royal College of Psychiatrists (College Report CR190, 2014), High Dose Antipsychotic Treatment (HDAT) is defined as the total daily dose of a single antipsychotic which exceeds the upper limit stated in the summary of product characteristics (SPC) or BNF, or a total daily dose of two or more antipsychotics which exceeds the SPC or BNF maximum using the percentage method, as illustrated below.

To determine the total percentage of the antipsychotic when there is more than one drug prescribed, the percentage of each drug should be calculated separately and then the results added together.

e.g. amisulpiride 400mg twice daily and olanzapine 15mg daily –

Amisulpiride – maximum daily dose 1200mg	– 100%
a daily dose 800mg is	- 67%
Olanzapine – maximum daily dose 20mg	– 100%
a daily dose of 15mg is	- 75%

Total daily percentage = 67% + 75% = 142% > 100% = high dose antipsychotic medication.

The majority of high-dose prescribing involves combined antipsychotics, including the prescribing of a second antipsychotic on a p.r.n. (as required) basis. The indication for which any p.r.n. medication is prescribed should be explicit and clearly documented and all p.r.n. medications should be reviewed on a regular basis. (CR190)

2 BACKGROUND

HDAT should only be used in exceptional circumstances because there is little convincing evidence that higher than recommended doses of antipsychotic drugs are more clinically effective than standard doses and the potential side effects are greater.

In practice there are several clinical scenarios where HDAT may be prescribed:

- Clozapine augmentation
- For short periods of combination antipsychotics (e.g. when changing medication)
- Use of strategies for managing challenging symptoms such as behavioural disturbance and aggression in people already prescribed regular antipsychotics.
- Progressive increments in dosage over time, where partial benefits are apparent
- Targeting a particular side effect or symptom with a second antipsychotic
- Where plasma levels are low and there is an established relationship between plasma levels and response

- Addition of oral antipsychotic treatment to a depot/long-acting injection to allow greater response and flexibility in dose titration
- People whose symptoms have responded inadequately to several trials of monotherapy at maximum doses

Problems associated with the use of HDAT include:

- Limited evidence of benefit.
- Greater risk of medication-related adverse events.
- Increase risk of drug–drug interactions.
- Poor medication adherence due to increased treatment complexity.

National Institute for Health & Clinical Excellence (NICE)

In its evidence review for the psychosis and schizophrenia guidelines NICE states that antipsychotics are usually prescribed within the recommended SPC dosage range and that there is little evidence to support the use of higher dosage or combination with another antipsychotic if monotherapy proves to be ineffective. According to the evidence the recommended dose ranges listed in the BNF and SPC are likely to achieve the best balance between therapeutic gain and dose-related adverse effects.

NICE CG178 advises that dosages outside the range given in the BNF or SPC should be justified and recorded.

For people with schizophrenia whose illness has not responded adequately to clozapine at an optimised dose, healthcare professionals may consider adding a second antipsychotic that does not compound the common side effects of clozapine to augment treatment.

Scottish Intercollegiate Guidelines Network (SIGN)

“There should not be routine use of multiple antipsychotic medications. Where polypharmacy is being considered in an individual clinical situation the benefits and harms should be discussed with the service user.

A trial of clozapine augmentation with a second generation antipsychotic should be considered for service users whose symptoms have not responded adequately to clozapine alone, despite dose optimisation. Treatment should be continued for a minimum of ten weeks.

Prescribing high dose antipsychotics should only be considered after adequate trials of antipsychotic monotherapy and augmentation, including a trial of clozapine, has failed”.

The British Association of Psychopharmacology (BAP)

"There does not seem to be any justification in the published literature for the use of high-dose antipsychotic medication for relapse prevention in schizophrenia.

Before resorting to high dosage, evidence based strategies for treatment-resistant illness should be exhausted, including optimised use of clozapine."

Pan Mersey Area Prescribing Committee Formulary

"Patients should not routinely receive high dose and/or combined antipsychotic medication due to increased risk of side effects. Exceptions must be evidenced based e.g. clozapine augmentation".

Summary

Use of HDAT should only be prescribed in exceptional circumstances where there is an explicit rationale and when other evidence-based strategies have failed.

HDAT should only be prescribed in the context of a carefully monitored, therapeutic trial after a risk–benefit assessment taking into account the greater risk of dose-related side effects.

3 RECOMMENDATIONS

<u>If a high-dose of an antipsychotic either single or in combination is being considered or is currently prescribed, it is advised to review the following first</u>:

- Review the diagnosis. (NICE CG178)
- Consider other causes of non-response, such as comorbid substance misuse (including alcohol), the concurrent use of other prescribed medication or physical illness.
- Ensure the compliance with current antipsychotic medication at a licensed therapeutically appropriate dose and duration.
- Consider checking drug levels where this is appropriate e.g. for clozapine, olanzapine to check for compliance and toxicity.
- Allow at least a 4-6 week period for each oral antipsychotic at a maximum licensed dose to assess response and tolerance (NICE CG178). Longer periods may be necessary for depots due to prolonged pharmacokinetics.
- If there is a poor response, or concern about side effects, consider switching to another antipsychotic and treat for an adequate therapeutic trial at optimum dose.

- If there is no response to at least 2 antipsychotics (at least one of them being a 2nd generation antipsychotic), consider prescribing clozapine.
- If there is an inadequate response to clozapine at optimal dose or poor tolerability, augmentation with an antipsychotic or other psychotropic agents may be beneficial. An adequate trial of clozapine augmentation may be up to 8–10 weeks. Choose a drug that does not compound the common side effects of clozapine. (NICE CG178)
- Considered possible adjuncts to antipsychotic treatment including antipsychotics (not exceeding the SPC or BNF maximum dose using the percentage method), mood stabilisers and anticonvulsants, antidepressants and benzodiazepines (NICE CG178). A trial of augmentation of antipsychotic treatment with antidepressants may be appropriate where negative symptoms persist beyond an acute episode of psychosis. Augmentation with lithium may be tried for patients with schizophrenia who exhibit affective symptoms (BAP 2011). Augmentation strategies may be tried for a specified therapeutic trial and discontinued if not beneficial.
- High-dose and combined antipsychotic treatment (which exceeds the SPC or BNF maximum using the percentage method) may be considered when antipsychotic monotherapy trials, optimised treatment with clozapine or other augmentation strategies, have been ineffective.
- The decision to use high-dose antipsychotic treatment should be made by a consultant psychiatrist based on benefit-risk assessment after discussing with multidisciplinary team and obtaining consent from the patient or carer if possible, alternatively seek an opinion from a second consultant psychiatrist
- The decision to use HDAT and rationale should be explicitly documented in the service user's clinical notes along with related monitoring and reviews.
- The use of high-dose antipsychotic medication should be treated as a limited therapeutic trial, with close monitoring of side effects and therapeutic response. The high dosage should be continued after 3 months only if there is evident clinical benefit that outweighs any risks (CR190). This risk-assessment of the HDAT should be clearly documented in the clinical notes.
- Risk assessment form should be completed (Appendix 1) following the necessary medical tests and investigations. All patients on high dose of antipsychotics should have regular ECG monitoring (at baseline, after each dosage increment, and every 6-12 months). (Maudsley Guidelines 13th ed.)
- The decision to use HDAT, service user informed consent (Appendix 2) and care plan should be fully documented in the clinical notes by the consultant.

4 RISK ASSESSMENT

4.1 Physical health

Before starting HDAT each service user should be reviewed at baseline for any physical health related issues to identify potential risks and help guiding the decision about treatment. Health checks should be performed before starting treatment and then at regular intervals and at least annually to ensure the maximum safety and efficacy of the treatment. Ideally, all the patients on high dose antipsychotic medication should have their renal function (urea & electrolytes; eGFR), liver function and ECG (electrocardiogram) monitored periodically to identify any clinically relevant changes or abnormalities.

Complete the relevant section on HDAT risk assessment and monitoring sheet (Appendix 1).

4.2 Drug interactions

Review the list of medication for all patients to identify any potential drug interactions. Refer to BNF or contact pharmacy or Medicines Information team for advice if necessary.

5 CONSENT AND AUTHORISATION

5.1 Consent

When HDAT treatment is being considered ideally the service user informed consent should be obtained and the service user consent form filled in (Appendix 2). If this is not possible this should be also documented on the same form. When T2 or T3 form is in place this must be updated as well.

5.2 Authorisation

Use of HDAT should be authorized by a consultant and documented in the clinical records. The information recorded should include reason for prescribing HDAT and the plan for monitoring and review.

6 MONITORING, REVIEW, FOLLOW-UP

- Where high-dose antipsychotics are prescribed, there should be a clear plan for regular clinical review including safety monitoring.
- Monitor efficacy of treatment and antipsychotic side effects using a combination of systematic enquiry (ideally use a validated rating scale), physical examination and appropriate haematological investigations.
- Each service user should have their physical health checked regularly. Tests may include: BMI/weight, BP, pulse, ECG, FBC, prolactin, U&Es and LFTs, blood lipids, HbA1c and fasting glucose. The results should be recorded on the HDAT risk assessment and monitoring sheet. (See Appendix 1).
- The clinical team responsible for patient care must ensure the relevant follow-ups are taking place both for inpatients and outpatients.
- The care plan and results of investigations should be shared with other health care professionals involved in the care of the patient where appropriate.

7 RESPONSIBILITIES

Project Team Role	Responsibilities
Doctors/Clinical team	The final decision on starting HDAT can only be made by a consultant psychiatrist, in consultation with the wider clinical team and the service user/carers, if appropriate. Identify service users on HDAT both on wards and in outpatient clinics and ensure the trust HDAT guidelines are followed and all relevant forms filled in as per procedure Ensure regular physical health monitoring takes place and the treatment is reviewed regularly for its effectiveness and side effects * Communicate with GPs and other health care professionals when the service user is under their care

Pharmacists	Identify that the patient is on high dose antipsychotics or has the potential for high dose when “prn” medication is taken into account Indicate on the drug chart if HDAT is in use Review drug chart for possible drug interactions Inform other staff members (nurses, doctors) of HDAT status and the trust HDAT procedure
Nursing staff	Be aware of patients on HDAT and the monitoring requirements, as per procedure Ensure that HDAT status is discussed at review

*Where the service user does not consent to HDAT monitoring but appears to have sufficient capacity regarding treatment the care plan should reflect this and the responsible clinician should weigh the risks and benefits of continuing treatment.

8 SUMMARY OF STANDARDS

- HDAT authorized by consultant.
- Informed consent sought where appropriate (appendix 2; T2/T3; care plan).
- Risk assessment completed (Appendix 1).
- Care plan agreed including relevant monitoring and review dates.
- High-dose antipsychotic (HDAT) should be endorsed on the drug chart/EPMA system.
- Monitoring carried out as per Appendix 1 or care plan.
- Efficacy and side effect assessed after a 3 month period with dosage returned to conventional levels after a 3-month period unless the clinical benefits evidently outweigh the risks.

9 PROCESS FOR MONITORING THIS PROCEDURE.

The Trust Drugs and Therapeutics Committee will periodically monitor compliance with this procedure.
A trust-wide baseline survey will be carried out initially to identify service users prescribed HDAT (inpatients and outpatients) and will be used to inform implementation.

Subsequently use of HDAT will periodically be monitored against the standards defined in this guideline.

This procedure will be subject to review on a regular basis. The next review is due in May 2019.

10 REFERENCES

1. Royal College of Psychiatrists: College Report CR190. Consensus statement on high-dose antipsychotic medication. November 2014. http://www.rcpsych.ac.uk/files/pdfversion/CR190.pdf

2. NICE: Psychosis and schizophrenia in adults: prevention and management. NICE guidelines [CG178], March 2014 https://www.nice.org.uk/guidance/cg178?unlid=567408697201621712245 6

3. SIGN 131: Management of schizophrenia, March 2013, accessed via: http://www.sign.ac.uk/pdf/sign131.pdf

4. Pan Mersey Area Prescribing Committee, Formulary Chapter 4: Central nervous system. http://formulary.panmerseyapc.nhs.uk/chaptersSubDetails.asp?FormularySectionID=4&SubSectionRef=04.02&SubSectionID=A100

5. BAP: Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology, 2011, accessed via https://www.bap.org.uk/pdfs/BAP_Guidelines-Schizophrenia.pdf

6. The Maudsley Prescribing Guidelines in Psychiatry. 13th Edition (2018). Taylor et al. Wiley Blackwell.

11 APPENDICES

Appendix 1. High dose antipsychotic therapy (HDAT) risk assessment and monitoring sheet

Appendix 2. Service user agreement to treatment with high dose antipsychotic therapy

AIDE MEMOIRE: HIGH DOSE ANTIPSYCHOTIC THERAPY (HDAT) RISK ASSESSMENT AND MONITORING *(Appendix 1)*

Results to be documented in the service users clinical notes and shared with the GP/relevant health care professionals

Patient name	Date of birth	Unit number	Consultant	Ward/Clinic

Check list: **1.** HDAT consent obtained/Form T2/T3 completed **2.** HDAT authorised by consultant and documented YES/NO

RISK ASSESSMENT Please circle risk factors	**Monitoring High Dose Antipsychotic Therapy: Minimum frequency - Baseline, at 3 months then 6 monthly thereafter**					
	Parameter	Baseline:.....(date)	3 months:.....(date)	.....:.....(date) When clinically relevant	.....(date) When clinically relevant	Annually** …..(date)
Cardiac condition? Y/N	Antipsychotic drugs prescribed including doses and frequencies					
Diabetes or glucose intolerance? Y/N	Total percentage of antipsychotic treatment					
Hyperlipidaemia? Y/N	Side effects assessed					
Renal impairment? Y/N	Response including adherence assessed***	N/A				
Hepatic impairment? Y/N	ECG					
Obesity? Y/N	Weight/BMI					
Epilepsy? Y/N	Pulse/BP					
Alcohol/illicit drug use? Y/N	Blood lipids					
Heavy smoker? Y/N	HbA1c					
Old age (>70)? Y/N	FBC (if appropriate)					
History of stroke/DVT? Y/N	U&Es					
History of HDAT Y/N	LFTs					
Other risk factors:	Prolactin					
	Other monitoring (as clinically indicated)					

Frequency of tests may differ depending on the clinical situation. The rationale of the monitoring should be reflected in the care plan.
****In line with current recommendations for physical health monitoring of people treated with antipsychotics ***Consider using any improvement scales such as CGI scale**

SERVICE USER AGREEMENT TO TREATMENT WITH HIGH-DOSE ANTIPSYCHOTIC THERAPY (*Appendix 2)*

May be completed by medical team for each patient before commencing treatment with high-dose antipsychotic medication.

NB: Consent may be recorded in the service user's clinical records or appropriate MHA forms used.

Service user name	Date of birth	Unit number	Consultant	Ward/Clinic

Diagnosis:……
……

Proposed treatment with high dose antipsychotic therapy: (drug, dose and rationale)
.....……
……

……

Service user has the capacity of making the decision about their treatment: YES/NO

If NO, appropriate legal framework followed: YES/NO

Service user/carer informed of:

- □ Benefits of clozapine explained
- □ Proposed HDTA and off label nature
- □ The purpose of the high-dose antipsychotic therapy
- □ Possible side-effects and health risks
- □ Required monitoring
- □ Next review date

Service user consent obtained: YES/ NO / N/A

If NO, appropriate legal framework followed: YES/NO

Service user statement (if the consent obtained):

I agree to the trial of the treatment with high-dose antipsychotic therapy

I understand the purpose of treatment and the possible risks associated with the therapy

Service user's signature……

Consultant's signature:……