NHS Grampian

Guidance For Staff Working Within The NHS Grampian Mental Health Service Relating To The Simultaneous Use Of More Than One Antipsychotic

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Organisational: Chief Executive and Management Teams
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Area: Line Managers
Hospital/Interface services: Assistant General Managers and Group Clinical Directors
Operational Management Unit: Unit Operational Managers
Policy statement: It is the responsibility of all staff to ensure that they are working to the most up to date and relevant policies, protocols procedures.

Review: This document will be reviewed in three years or sooner if current treatment recommendations change.

Responsibilities for review of this document:

Responsibilities for ensuring registration of this document on the NHS Grampian SharePoint:	Principal Pharmacist, Mental Health and Learning Disability Services
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August 2023	January 2020	Introduction – New section as per new template.	P2, 1 - Introduction
August 2023	January 2020	Objective - New section as per new template.	P2, 1.1 - Objective
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August 2023	January 2020	Clinical Situations - New section as per new template.	P2, 1.3 - Clinical Situations
August 2023	January 2020	Patient Groups To Which This Document Applies - New section as per new template.	P2, 1.4 - Patient Groups To Which This Document Applies
August 2023	January 2020	Evidence Base - New section as per new template. Evidence updated in line with The Maudsley Prescribing Guidelines 14th Edition, 2021.	P2, 2 - Evidence Base
August 2023	January 2020	References updated.	P4, 4 - References
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1 Introduction

In psychiatric practice, prescriptions for combined antipsychotic medications are not uncommon. National clinical audits conducted by the Prescribing Observatory for Mental Health (POMH-UK)[1] have found that the most common reasons for prescribing combined antipsychotics were a poor response to antipsychotic monotherapy and cross titration from one antipsychotic to another. The use of combined antipsychotics has been found to be associated with younger patients, males, those with severe and chronic illness, hospital in-patients and a diagnosis of schizophrenia. However, there is a lack of robust evidence that the efficacy of combined antipsychotics is superior to treatment with a single antipsychotic. In addition there is substantial evidence supporting the potential for harm and so the use of combined antipsychotic medications, which is commonly a high-dose prescription, should generally be avoided.[2]

1.1 Objective

To provide prescribing guidance for staff working in Mental Health and Learning Disability Services relating to the simultaneous use of more than one antipsychotic medication.

1.2 Definitions

The simultaneous use of more than one antipsychotic is defined as one or more antipsychotics prescribed at the same time.

1.3 Clinical Situations

The simultaneous use of more than one antipsychotic can occur in one of three ways:

- During cross titration of antipsychotic medications.
- During periods of acute psychosis when additional doses of antipsychotic may be given on an ‘as required’ basis, as pre-rapid tranquillisation or rapid tranquillisation.
- The use of more than one regularly prescribed antipsychotic medication, usually clozapine and another antipsychotic, where there has been a partial response to monotherapy or dose-limiting side-effects.

1.4 Patient Groups To Which This Document Applies

This guidance applies to in-patients and out-patients of Mental Health and Learning Disability Services (MHLDS).

2 Evidence Base

There is a lack of robust evidence supporting the efficacy of combined, non-clozapine antipsychotic medications. The evidence base supporting such combinations consists, for the most part, of small open label studies and case series.[2] A meta-analysis of antipsychotic augmentation of clozapine indicates a very small effect overall.[3] In addition a randomised, double-blind, placebo controlled trial supports the use of aripiprazole augmentation of clozapine to reduce body weight[4] and a systematic review and meta-analysis provides evidence for the use of aripiprazole augmentation to normalise prolactin levels in those on haloperidol and risperidone.[5]

In addition, a non-interventional, population based study in Hungary, compared the effectiveness of antipsychotic monotherapy with combined antipsychotic therapy over a one year period. This study found that while monotherapy was superior in efficacy to combined antipsychotic treatment, polypharmacy was associated with lower mortality and psychiatric hospitalisations.[6] Another observational study conducted in Finland over a 20 year period found that antipsychotic combinations, particularly those with clozapine or long-acting antipsychotic injections were associated with slightly lower rates of hospitalisation compared to monotherapy.[7] It may therefore be that combining antipsychotic medications with different receptor specificities may be more effective and lead to better efficacy and tolerability.[2]

In contrast there is substantial evidence supporting the potential for harm with combined antipsychotic medications. Clinically significant side-effects include increased risk of extrapyramidal side-effects, metabolic side-effects and diabetes, sexual dysfunction, increased risk of hip fracture, paralytic ileus, grand mal seizures, QT-interval prolongation and arrhythmias.[2]

3 Recommendations

3.1 Points to consider:

- The routine prescribing of more than one antipsychotic medication at a time may be best avoided unless in exceptional circumstances (e.g. clozapine augmentation or when changing medication during titration).
- The risk of drug interactions and other adverse events is increased.
- Treatment with more than one antipsychotic is complex and potentially confusing.
- High dose antipsychotic prescribing can inadvertently occur with combinations (particularly with “as required” medication), i.e. when the sum of the percentage of the British National Formulary (BNF) maximum dose for each antipsychotic exceeds 100%.
- Treatment with more than one antipsychotic can make it difficult to accurately titrate the doses of each drug and to assess their individual effectiveness.
- Some antipsychotic polypharmacy (e.g. combinations with aripiprazole) shows clear benefits for tolerability but not efficacy.

3.2 Actions to take before prescribing more than one antipsychotic at a time

Ensure that:

- The current diagnosis is correct.
- Patient has been compliant with previous/current treatment.
- Dose and duration of previous/current treatment has been adequate.
- Adverse social and psychological factors have been minimised.
- Alternative adjunctive drug therapies (e.g. mood stabilisers, anxiolytics and antidepressants) have been tried.
- Avoid confusing sedative effect with antipsychotic effect.
- An objective measure of effectiveness of drug therapy on symptomatology is used, e.g. Clinical Global Impression (CGI).
- Where a clinical improvement occurs before a switch from one antipsychotic to another is complete, continue with treatment plan until the switch is complete and monotherapy achieved.

3.3 When it is appropriate to prescribe combination antipsychotics

Note: The decision to prescribe more than one antipsychotic should only be taken as part of a considered treatment plan, following multidisciplinary review, with the rationale and outcome clearly documented in the patient's medical notes. The prescribing of more than one antipsychotic may be appropriate where the following criteria apply:

- During cross titration when switching from one antipsychotic to another.
- As a temporary measure during a period of acute exacerbation of illness when additional doses of antipsychotic may be given on an 'as required' basis, as pre-rapid tranquillisation or rapid tranquillisation.
- For patients who have:
    - Been unable to tolerate higher doses of clozapine.
    - Shown only a partial response to clozapine.

3.4 Minimum requirements if combination antipsychotics are prescribed

- The rationale for use should be documented in the patient's clinical notes.
- The patient should be informed, consent obtained and recorded in the clinical notes. If the patient refuses consent then the use of Mental Health (Care and Treatment), (Scotland) Act 2003 will need to be considered. If the patient is incapable of giving informed consent, use of the Adults with Incapacity (Scotland) Act 2000 may be required. Also consider any advance statement the patient may have made.
- The use of combination antipsychotic therapy should be reviewed regularly with regard to the clinical indication and any beneficial effect on symptoms documented.
- All patients should be systematically monitored for adverse effects (including an Electrocardiogram (ECG)) which should be carefully documented.

- If no improvement is seen at review, discontinuation of multiple antipsychotic therapy should be considered.
- If a combination will result in high dose antipsychotic prescribing (i.e. when the sum of the percentage of the BNF maximum dose for each antipsychotic exceeds 100%), refer to the Guidance For Staff Working In The Mental Health Service For The Use of High-dose Antipsychotic Therapy (HDAT) and see Appendix 1 for Identification of Patients on HDAT; Appendix 2 for HDAT Monitoring Responsibilities; Appendix 3 for HDAT Initial Monitoring Form and Appendix 4 for HDAT Continuation Form.

4 References

1. Prescribing Observatory for Mental Health. Topic 1g and 3d. Prescribing high dose and combined antipsychotics on adult psychiatric wards. 2017; Prescribing Observatory for Mental Health CCQI1272.
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5. Correll, CU, et al. Selective effects of individual antipsychotic co-treatments on cardio-metabolic and hormonal risk status: results from a systematic review and meta-analysis. *Schizophr Bull* 2013; **39** (Suppl 1):S29-S30.
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5 Distribution list

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