CLINICAL GUIDELINES FOR THE PHARMACOLOGICAL MANAGEMENT OF ACUTELY DISTURBED BEHAVIOUR

CLINICAL GUIDELINE REFERENCE NUMBER: CG52
VERSION NUMBER: 4
REPLACES SEPT DOCUMENT: CG52
REPLACES NEP DOCUMENT: MedsPol/Tab19
KEY CHANGES FROM PREVIOUS VERSION: Drug choice / non-prone restraint / algorithm for dementia / non-contact physical monitoring.
AUTHOR: Chief Pharmacist / Senior Pharmacist for Governance
CONSULTATION GROUPS: Medicines Management Group (Mental Health & Learning Disabilities)
IMPLEMENTATION DATE: 1st July 2017
AMENDMENT DATE(S): 5th December 2019
LAST REVIEW DATE: January 2020
NEXT REVIEW DATE: January 2023
APPROVAL BY CLINICAL GOVERNANCE AND QUALITY SUB COMMITTEE: 22nd January 2020

CLINICAL GUIDELINE SUMMARY
These clinical guidelines aim to ensure that staff are provided with current information and underpinning principles considered by the Trust to be essential regarding the pharmacological treatment of acutely disturbed behaviour.

The principles contained within this clinical guideline and associated documents aim to ensure that open communication and respect are fundamental elements of the management of violence and aggression.

The Trust monitors the implementation of and compliance with this clinical guideline in the following ways:
Procedures for the pharmacological management of acutely disturbed behaviour will be included in the three year Medicines Management audit programme. The results will be presented Medicines Management Group for review and identification of any actions required.

SCOPE

<table>
<thead>
<tr>
<th>Services</th>
<th>Applicable</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trustwide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental Health &amp; Specialist Services</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Community Health Services</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Director responsible for monitoring and reviewing this Clinical Guideline is The Executive Medical Director
CONTENTS

This is an interactive contents page, by clicking on the titles below you will be taken to the section that you want.

1.0 INTRODUCTION

2.0 SCOPE

3.0 DEFINITION

4.0 RESPONSIBILITIES

5.0 UNDERPINNING PRINCIPLES

6.0 DRUGS USED FOR THE PHARMACOLOGICAL TREATMENT OF ACUTELY DISTURBED BEHAVIOUR

7.0 ROUTES OF ADMINISTRATION

8.0 PRE-TREATMENT CHECKS

9.0 ADDITIONAL FACTORS TO CONSIDER WHEN PRESCRIBING

10.0 CLINICAL MONITORING OF VITAL SIGNS

11.0 ENTRIES INTO CLINICAL NOTES

12.0 AFTER THE TREATMENT OR ACUTELY DISTURBED BEHAVIOUR

13.0 REMEDIAL MEASURES

14.0 USE OF FLUMAZENIL FOR BENZODIAZEPINE REVERSAL

15.0 USE OF ZUCLOPENTHIXOL ACETATE (CLOPIXOL ACUPHASE®)

16.0 AIMS

17.0 RESPONSIBILITIES

18.0 IMPLEMENTATION

19.0 PHARMACOLOGICAL AGENTS

20.0 TRAINING
21.0 CLINICAL GUIDELINE REVIEW

22.0 REFERENCES

ANNEXES

ANNEX 1 - Effects of antipsychotics on QTc / Cautions for haloperidol / Effect of promethazine on QTc

ANNEX 2 - Recommendations on injection site for common IM drugs.

APPENDICES

APPENDIX 1 - MANAGEMENT OF ACUTELY DISTURBED PATIENTS (ADULTS)

APPENDIX 2 - MANAGEMENT OF ACUTELY DISTURBED PATIENTS (OLDER PEOPLE - EXCLUDING DEMENTIA)

APPENDIX 3 - MANAGEMENT OF ACUTELY DISTURBED PATIENTS (DEMENTIA SERVICES)

APPENDIX 4 - MANAGEMENT OF ACUTELY DISTURBED PATIENTS (CHILDREN & ADOLESCENTS)
1.0 INTRODUCTION

1.1 The pharmacological treatment of acutely disturbed behaviour is a strategy used to manage the high risk of imminent violence. The aim of this treatment is to achieve a state of calm sufficient to minimise the risk posed to the patient or to others, without excessive sedation/sleep.

1.2 The Trust believes that preventive strategies and measures such as engagement and the development of therapeutic relationships based on respect are basic elements underpinning this clinical guideline and sets out the principles and procedures through which the pharmacological management of acutely disturbed behaviour will be handled within the Trust.

1.3 Violence amongst psychiatric inpatients is predicted by florid psychotic symptoms, particularly disorganisation symptoms, mania, lack of insight, anger, hostility, and drug or alcohol intoxication.

1.4 Imminence of violence may be suggested by rapidly increasing verbal aggression or anger, possibly associated with explicit threats of violence, changes or extremes of behaviour or outward signs of inter tension.

1.5 The use of sedative medication is one of several strategies commonly used in the management of severely disturbed behaviour in inpatient settings. Others include de-escalation, distraction techniques, physical restraint and seclusion.

1.6 The severity of the disturbed behaviour, associated risk to the patient or to other people, and the imminence of that risk, determines the strategies to be employed in a particular situation. Where the risk is assessed as both severe and imminent, treatment with medicines may be employed.

1.7 Service users who participated in the Royal College of Psychiatrists Research Unit’s discussion group reported that when they behaved violently, medication was their preferred option compared with seclusion or prolonged physical restraint. Treatment with medicines in these situations is often viewed as punitive by patients.

1.8 Treatment of acutely disturbed behaviour with medicines has a limited evidence base because clinical trials in this area are difficult to conduct. The British Association for Psychopharmacology and the National Association of Psychiatric Intensive Care and Low Secure Units recently published their joint evidence-based consensus guidelines for the clinical management of acute disturbance: de-escalation and rapid tranquilisation, and these provide a useful overview of best practice. This Trust guideline provides medical and nursing staff with information that will allow them to make appropriate clinical decisions based on the characteristics of the individual patient and situation.
This procedural guideline also takes into account National Institute for Health and Clinical Excellence (NICE) guidelines on psychosis and schizophrenia in adults: prevention and management, NICE guidelines on Violence and Aggression: short-term management in mental health, health and community settings, NICE guidelines on Bipolar disorder: Assessment and management, NICE guidelines on antenatal and postnatal mental health: Clinical management and service guidance, and the independent inquiry into the death of David Bennett.

The procedural guideline for restrictive practice (RMPG05) should be consulted for detailed guidance on general preventative measures, primary de-escalation interventions and managing restraint, which should be considered to be a last resort.

### 2.0 SCOPE

2.1 This clinical guideline applies to all employees (both permanent and temporary) of the Trust. Only doctors and qualified nursing staff are authorised to prescribe/administer, respectively, medication for the pharmacological management of acutely disturbed behaviour.

2.2 Administration of medication for the pharmacological management of acutely disturbed behaviour will only be used within the adult acute wards, older people’s acute wards PICU and forensic wards; the inpatient CAMHS units; and Wood Lea, and Heath Close within the Learning Disability Service.

2.3 The clinical guideline complements all professional and ethical rules, guidelines and codes of professional conduct.

2.4 This clinical guideline must be read in conjunction with the following policies:

- CG6 Clinical Guidelines for Advance Decisions and Statements for Adults
- CLP14 Policy for cardio-pulmonary resuscitation (CPR)
- RM05 Restrictive Practice Policy
- CLP41 Seclusion and Long Term Segregation Policy

The relevant section of the Trust Formulary and Prescribing Guidelines on the pharmacological management of acutely disturbed behaviour should also be consulted.

### 3.0 DEFINITION

3.1 ‘Acute disturbance’ is defined as an acute mental state associated with an underlying mental and/or physical disorder in the form of: (i) agitation and distress, which is excessive verbal or motor activity that may or may not lead to aggression or violence; or (ii) actual aggression or violence entailing harm, hurt or injury to another person, or damage to property regardless of whether it is verbally or behaviourally expressed, physical harm is sustained, or the intention is clear.
3.2 The pharmacological management of acutely disturbed behaviour encompasses a number of strategies involving pharmacological intervention:

- Pre-RT (pre rapid tranquilisation). This refers to the time period when oral medicine is administered. This may be the only pharmacological intervention, although in some cases rapid tranquilisation (RT) will be administered subsequently.\(^\text{10}\)

- Rapid Tranquilisation (RT). Its goal is to achieve a state of calmness without sedation, sleep or unconsciousness, thereby reducing the risk to self and/or others while maintaining the ability of the patient to respond to communication\(^\text{11}\). However, for acute disturbance, sedation may also be considered to be an appropriate interim strategy\(^\text{1}\). RT is defined by NICE as parenteral, rather than oral – “RT: use of medication by the parenteral route (usually intramuscular or, exceptionally, intravenous) if oral medication is not possible or appropriate and urgent sedation with medication is needed.”\(^\text{1}\)

3.3 The aims of management are three-fold\(^\text{3}\):

- to reduce suffering for the patient – psychological or physical (through self-harm or accidents)
- to reduce risk of harm to others by maintaining a safe environment
- to do no harm (by prescribing safe regimens and monitoring physical health)

3.4 All medication given in the urgent management of severely disturbed/violet behaviour including pro re nata (PRN) medication should be administered from an agreed protocol or as part of an advance directive.

3.5 NICE have defined “PRN” as “the use of medication as part of a strategy to de-escalate or prevent situations that may lead to violence or aggression; it does not refer to PRN medication used on its own for rapid tranquilisation during an episode of violence of aggression.

4.0 RESPONSIBILITIES

4.1 The Executive Director of Mental Health and Deputy Chief Executive will ensure:

- Clinical Guidelines are embedded into clinical practice as well as the best practice framework and ensure that these are updated regularly
- the identification and implementation of training and educational needs arising from any relevant documentation

4.2 Directors and Senior Management will:

- monitor the implementation of this clinical guideline via clinical audit and supervision
• ensure that the Trust Risk Management team is appropriately notified of all incidents
• Be able to evidence that EPUT clinical guidelines have been followed.

4.3 Lead Trainers for PMVA, Medicines Management and Enhanced Emergency Skills will:

• ensure that any changes in professional knowledge and practice are regularly discussed and updated
• ensure that all Trust teams are appropriately notified of all current information on practice
• ensure training is delivered and monitored with records continually updated
• encourage staff to discuss any issues related to the management of acutely disturbed behaviour during clinical supervision

4.4 Ward Managers/Charge Nurses will:

• ensure that these clinical guidelines are followed
• ensure that all patient safety incidents are reported on the Datix form in line with the requirements of Trust policy CP3.
• ensure staff receive appropriate and correct training in line with Trust requirements
• ensure any Advance Statement/ Parental Consent are considered and used if appropriate
• Monitor the use of treatment of acutely disturbed behaviour as an essential part of managing their clinical area. They will collate reports to relevant groups and committees ensuring individual instances are objectively reviewed and audit undertaken
• ensure that patients who have received treatment of acutely disturbed behaviour are supervised/monitored by qualified nursing staff in line with this procedural guideline
• ensure issues relating to treatment of acutely disturbed behaviour are discussed during clinical supervision

4.5 Individual staff will:

• adhere to this procedural guideline
• Undertake appropriate and approved training

5.0 UNDERPINNING PRINCIPLES

5.1 The need for treatment of acutely disturbed behaviour requires careful clinical judgement. Treatment of acutely disturbed behaviour should not be carried out without an assessment of the physical health of the patient, non-chronological age (frailty), and consideration of concurrent medication. In
particular the presence of delirium or intoxication should be considered before treatment is commenced.

5.2 The consultant psychiatrist and multidisciplinary team, including a specialist clinical pharmacist, should undertake a full assessment. Extra care should be taken in the following circumstances:

- the presence of prolonged QTc syndromes
- the concurrent use of medication that lengthens the QTc interval (see Annex 1 for a list of drugs known to prolong QT interval)
- the presence of certain disorders affecting metabolism, e.g. dehydration, hypo/hyperthermia, stress, extreme emotion, extreme physical exertion, physical illness and dementia

5.3 Attention should be given to advance directives or parental consent if appropriate.4

5.4 The dose of medication must be individualised for each patient. The prescription will depend on several factors including age, non-chronological age (frailty), associated physical disorders, and other medication prescribed.

5.5 Treatment of acutely disturbed behaviour is potentially hazardous. Medical support should normally be available, and attendance of medical staff required if requested by the nurse in charge when this treatment is undertaken, in order to deal with adverse drug reactions, over sedation or the need to reverse benzodiazepine-induced respiratory depression through the administration of intravenous flumazenil.

5.5.1 Resuscitation equipment must be available and easily accessible (within 3 minutes) at sites where treatment of acutely disturbed behaviour may be undertaken. Equipment available must include an automatic external defibrillator, a bag valve mask, oxygen and suction equipment. All equipment must be properly maintained and checked on a weekly basis, and a record maintained.

5.5.2 Procyclidine injection must be available before treatment is commenced.

5.5.3 Flumazenil must be available at all sites, wherever parenteral benzodiazepines are prescribed10.

5.5.4 In the event of a medical emergency, for example respiratory compromise, where a doctor is not available to attend, an ambulance should be requested via the normal ‘999’ route.

5.6 Plans for the management of individual patients should, ideally, be made in advance with the aim of preventing disturbed behaviour and reducing the risk of violence. Nursing interventions (de-escalation), increasing nursing levels, transfer to a PICU and pharmacological strategies are all options that may be employed.3
5.7 Some patients may express a particular preference through an advance directive for the medication they wish to be considered, or other strategies to be utilised in managing their aggression. These should be respected, although health and safety consideration may determine that other methods of treatment are used.

5.8 All staff need to be aware of the legal framework that authorises the use of treatment of acutely disturbed behaviour, physical intervention and seclusion. The guidance of the Mental Health Act Code of Practice\textsuperscript{18} should be followed, with any departures clearly recorded and justified as being in the patient’s best interest.

Mental Health Act Code of Practice\textsuperscript{18} paragraph 26.99 states:

“Physical restraint may, on occasion, need to be used to administer rapid tranquillisation by IM injection to an unwilling patient, where the patient may lawfully be treated without consent. It must not be used unless there is such legal authority, whether under the Act, the MCA or otherwise. Rapid tranquillisation must not be used to treat an informal patient who has the capacity to refuse treatment and who has done so.”

6.0 DRUGS USED FOR THE PHARMACOLOGICAL TREATMENT OF ACUTELY DISTURBED BEHAVIOUR

6.1 The BAP/NAPICU\textsuperscript{10} treatment recommendations are summarised below, with their efficacy and safety concerns, together with the categories of evidence (I to IV), and strength of recommendation (A-D, S).

Pre-RT: Oral, oral-inhaled and buccal.

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral lorazepam may be effective (IV; D).</td>
<td></td>
</tr>
<tr>
<td>Oral promethazine may be effective (S).</td>
<td></td>
</tr>
<tr>
<td>Oral formulations of aripiprazole, olanzapine and risperidone are effective (Ib; A).</td>
<td>Aripiprazole has a slow onset, which needs to be considered.</td>
</tr>
<tr>
<td>Oral haloperidol is effective and a baseline ECG is advised before use due to the risk of QTc prolongation (III; C).</td>
<td></td>
</tr>
<tr>
<td>Oral quetiapine is effective (III; C).</td>
<td></td>
</tr>
<tr>
<td>Oral-inhaled loxapine is effective although a brief respiratory assessment is required beforehand, as it is contraindicated in patients with asthma or chronic obstructive pulmonary disease, and a short-acting beta-agonist bronchodilator (e.g. salbutamol) should be available (Ib; A).</td>
<td>Not formulary</td>
</tr>
</tbody>
</table>
Buccal midazolam is effective (III; C). | Not formulary

<table>
<thead>
<tr>
<th>NOT RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral formulations of clonazepam and diazepam are <strong>not recommended</strong> due to lack of evidence for use in RT together with the risk of accumulation with repeated dosing and the resultant risk of cumulative adverse effects (S).</td>
</tr>
<tr>
<td>Oral levomepromazine is <strong>not recommended</strong> due to lack of evidence for use in RT (S).</td>
</tr>
</tbody>
</table>

RT: **IM monotherapy.**

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM lorazepam is effective (Ib; A).</td>
<td></td>
</tr>
<tr>
<td>IM promethazine may be effective (extrapolated Ia; D)</td>
<td>Not licensed for RT, but supported by evidence in NICE and BAP. Use with caution in LD and dementia due to its anticholinergic effects</td>
</tr>
<tr>
<td>IM aripiprazole is effective (Ia; A).</td>
<td>Supported by BAP. Not included in NICE recommendations.</td>
</tr>
<tr>
<td>IM olanzapine is effective, but it should only be administered by itself and not concurrently with IM benzodiazepines due to risk of hypotension, sedation and cardiorespiratory depression; thus, there should be an interval of at least 1 hour between the two (Ia; A).</td>
<td>Caution</td>
</tr>
<tr>
<td>RT IM monotherapy should be considered before RT IM combinations</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NOT RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM clonazepam is <strong>not recommended</strong> due to a relative lack of supporting evidence for use in RT (S).</td>
</tr>
<tr>
<td>IM diazepam is <strong>not recommended</strong> due to lack of evidence for use in RT (S).</td>
</tr>
</tbody>
</table>

IM diazepam has erratic absorption;
its effect may be unpredictable and potentially overwhelming.

IM midazolam is **not recommended** due to the risk of respiratory depression (Ia; A).

IM haloperidol is **not recommended** as monotherapy even though it has evidence of effectiveness, and a baseline ECG is advised, as measures need to be in place to offset its adverse effects and especially for the risk of acute dystonia (Ia; A).

IM levomepromazine is **not recommended**, even though it has some evidence of effectiveness, as there is potential evidence for a risk of cardiovascular adverse effects, especially hypotension (III; C).

**RT**: IM combinations.

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM promethazine plus IM haloperidol is <strong>effective</strong> and a baseline ECG is advised before haloperidol use due to the risk of QTc prolongation (Ia; A).</td>
<td></td>
</tr>
<tr>
<td>IM lorazepam plus IM haloperidol is <strong>effective</strong> and a baseline ECG is advised before haloperidol use due to the risk of QTc prolongation (Ia; A).</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NOT RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM lorazepam plus IM promethazine is <strong>not recommended</strong> due to lack of evidence for efficacy for this combination (S).</td>
</tr>
</tbody>
</table>

**RT**: IV monotherapy.

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both IV lorazepam and IV midazolam are effective (Ib; A).</td>
<td></td>
</tr>
<tr>
<td>IV olanzapine has evidence of effectiveness but caution is advised due to the risk of respiratory depression and the lack of a reversing agent (III; C).</td>
<td>Caution</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NOT RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV diazepam is not recommended due to lack of evidence for use in RT (S).</td>
</tr>
<tr>
<td>IV haloperidol is not recommended due to a lack of evidence for its use in RT (S).</td>
</tr>
</tbody>
</table>
Non-response to pre-RT and RT interventions.

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seeking senior advice, conducting a comprehensive case review and a reviewing the appropriateness of the clinical setting should all be considered (S).</td>
<td></td>
</tr>
<tr>
<td>Zuclopenthixol acetate is not recommended for use as RT as the evidence does not support it, particularly as its onset of action takes several hours. However, after other strategies have failed to achieve a required response, its use may be considered. A baseline ECG is advised before use due to the risk of QTc prolongation (III; C).</td>
<td></td>
</tr>
<tr>
<td>ECT may also be considered when other strategies have failed to achieve a required response, and particularly if the underlying disorder has an evidence base for the use of ECT (e.g. mania) or if there is a history of good response for the individual patient (IV; D).</td>
<td></td>
</tr>
<tr>
<td>IM ketamine is effective but it is not recommended due to risk of respiratory depression (III; C).</td>
<td></td>
</tr>
</tbody>
</table>

6.2 Choice of medicine for RT

6.2.1 Based on the review of RT above, the evidence suggests that two strategies may have benefits that outweigh risk of harm:

- an IM benzodiazepine (lorazepam) used alone
- a combination of IM haloperidol plus IM promethazine. (This combination may reduce EPSE).

While IM haloperidol is effective alone, its side effect profile means that it is not recommended as a monotherapy.

6.2.2 The combination of IM benzodiazepine plus IM haloperidol does not appear to be more effective than IM benzodiazepine alone. But the combination is still effective.

6.2.3 Olanzapine IM is effective, and remains an option; although there is no UK-licensed product, EU-licensed products are still available.

6.3 Choosing a drug for RT for an individual patient

6.3.1 Use either intramuscular lorazepam on its own or intramuscular haloperidol combined with intramuscular promethazine for rapid tranquillisation in adults.

6.3.2 If there is insufficient information to guide the choice of medication for rapid tranquillisation, or the service user has not taken antipsychotic medication before, use intramuscular lorazepam.
6.3.3 If there is evidence of cardiovascular disease, including a prolonged QT interval, or no electrocardiogram has been carried out, avoid intramuscular haloperidol combined with intramuscular promethazine and use intramuscular lorazepam instead.

A baseline ECG is advised before haloperidol use (in any formulation) due to the risk of QTc prolongation. It is therefore advised, as the licence for haloperidol recommends, that a baseline ECG should available before administering IM haloperidol. Consequently, as it is often not possible in the scenario of acute disturbance to carry out an ECG, and if one has not been done recently, haloperidol should be avoided, and an alternative IM drug used. If haloperidol is used when no ECG is available the prescriber should consider the risks and benefits of using this treatment and be able to justify their prescribing decision as this would be considered an ‘off-label use’. Where possible, and where facilities exist, ECG monitoring is strongly recommended whenever antipsychotics are administered and especially where high doses or parenteral route are be used. High stress levels, restraint, agitation, and hypokalaemia all place the patient at high risk of developing cardiac arrhythmias. As a minimum, ECG’s need to be less than 3 months old to be considered appropriate for use assuming there have been no significant cardiac changes since the ECG was obtained. Preferably ECG monitoring should happen as close to the RT as possible.

6.3.4 If there is a partial response to intramuscular lorazepam, consider a further dose.

6.3.5 If there is no response to intramuscular lorazepam, consider intramuscular haloperidol combined with intramuscular promethazine.

6.3.6 If there is a partial response to intramuscular haloperidol combined with intramuscular promethazine, consider a further dose.

6.3.7 If there is no response to intramuscular haloperidol combined with intramuscular promethazine, consider intramuscular lorazepam if this hasn't been used already during this episode. If intramuscular lorazepam has already been used, arrange an urgent team meeting to carry out a review and seek a second opinion if needed.

6.4 Prescribing

6.4.1 When deciding which drug to use, take into account:

- the service user's preferences or advance statements and decisions
- pre-existing physical health problems or pregnancy
- possible intoxication
- previous response to these medications, including adverse effects
- potential for interactions with other medications
- the total daily dose of medications prescribed and administered
- cumulative antipsychotic dose per day, including regular medication and any depot that may have been administered during the period within which it remains active
• use of RT in patients receiving clozapine (additional antipsychotic may increase cardiac and haematological risks)
• use of RT in patients receiving lithium (risk of neurotoxicity with haloperidol)

The Mental Health Act Code of Practice\textsuperscript{18} states in paragraph 26.97: “Where a prescription indicates a choice of administration routes for rapid tranquillisation (e.g. oral or IM injection), the person prescribing the medication should list factors which should be considered in deciding which route to use under any reasonably foreseeable circumstances”.

6.4.2 Prescribing oral

6.4.2.1 The reason for prescribing should be documented in the clinical record, including the treatment plan and any recommended monitoring.

6.4.2.2 Where prescribed in the context of pre-RT treatment, the indication on the treatment chart should be clearly endorsed as “severe agitation and anxiety only”.

6.4.2.3 Do not prescribe any oral PRN medication(s) routinely or automatically on admission on the ‘as required’ section of the drug chart.

6.4.2.4 Where clinically indicated, ensure oral prn medication for acute & severe agitation is prescribed on the “as required” section of the drug chart and prescribe initially for a maximum of 96 hours.

6.4.2.5 Only when oral prn medication for acute & severe agitation oral medication continues to be required should it be prescribed beyond the initial 96 hours on the ‘as required’ section of the drug chart. Including indication, maximum dose, interval and maximum daily dose. This should be reviewed at least once weekly and if not used within the last 2 weeks, consider stopping it.

6.4.2.6 Oral prn medication for acute & severe agitation should only be offered after non-drug de-escalation techniques have not been successful, and before IM medication is considered.

6.4.2.7 If more than one medication is prescribed, the care plan should include the preferred order of administration of medicines and time interval between the medicines.

6.4.2.8 If two medications are intended to be given at the same time this should be clearly stated.
6.4.3 Prescribing RT (parenteral)

6.4.3.1 The reason for prescribing should be documented in the clinical record, including the treatment plan.

6.4.3.2 Do not prescribe RT medication routinely or automatically on admission on the drug chart. NICE guidance states that RT should initially only be a single dose. When RT is deemed clinically appropriate, initial dose(s) must be prescribed as a stat dose within the “once only” section of the drug chart, and the reason recorded in the patient clinical record.

6.4.3.3 After reviewing the effect of any initial stat dose, further doses can be re-prescribed if essential, as either further stat doses, or in the “PRN antipsychotics” section of the drug chart. RT should only be re-prescribed when deemed appropriate to continue. This should be reviewed at least once weekly and if not used within the last two weeks, consider stopping it. Antipsychotics prescribed as PRN for RT should be reviewed at least once weekly and if not used within the last one week, consider stopping it. (Whether they are used in the framework of RT, pre-RT, or non-RT, all antipsychotics prescribed PRN are to be reviewed after six PRN doses or 7 days).

6.4.3.4 If more than one medication is prescribed, the care plan should include the preferred order of administration of medicines and time interval between the medicines.

7.0 ROUTES OF ADMINISTRATION

7.1 Oral medication should always be offered before parenteral medication.\(^4\)

7.2 If parenteral administration proves necessary, the intramuscular (IM) route should be preferred over the intravenous route.\(^4\) Absorption after IM administration can occur far more rapidly when the patient is agitated, excited or physically overactive.\(^1\)

7.3 Intravenous (IV) administration should only be used in exceptional circumstances. This decision should be made by a consultant psychiatrist and not by junior medical staff.\(^4\)

<table>
<thead>
<tr>
<th>Route</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Safest, but slow onset of action compared with parenteral (except for lorazepam, where oral and IM have similar speed of onset)</td>
</tr>
<tr>
<td>IM</td>
<td>Faster onset of action than oral route (except lorazepam). Injection may be painful and absorption can be erratic</td>
</tr>
<tr>
<td>IV</td>
<td>Provides rapid onset of action, but potentially hazardous and not recommended except in exceptional circumstances. Consultant involvement mandatory. Requires resuscitation facilities and suitably trained staff to be available. Nursing staff not permitted to administer drugs intravenously</td>
</tr>
</tbody>
</table>
7.4 If combinations of injections are used they should not be mixed together in the same syringe.¹

7.5 There is a drive internationally to reduce restrictive practices. In the UK, there is a government directive¹² to reduce all forms of restrictive practices, with an objective of ending the use of prone (face-down) restraint; restrictive practices should only be used as a last resort in emergency situations.

“People must not be deliberately restrained in a way that impacts on their airway, breathing or circulation. The mouth and/or nose must never be covered and techniques should not incur pressure to the neck region, rib cage and/or abdomen. There must be no planned or intentional restraint of a person in a prone/face down position on any surface, not just the floor.”¹²

The Mental Health Act Code of Practice¹⁸ states in paragraph 26.98:

“Where rapid tranquilisation in the form of an IM injection is needed, the person prescribing the injection should state the preferred injection site, having taken full account of the need to avoid prone restraint…”

Consideration should be given to the choice of restraint positions (prone / supine (face-up) / semi-seated), to the choice of techniques and equipment (e.g. safety pods) and suitable injection sites.

Annex 2 lists the intramuscular sites specified in the summary of product characteristics for the common medicines used in rapid tranquilisation. This list should be referred to when choosing a site to administer the intramuscular injection.

Sites for IM injection, and their recommended maximum volumes of fluid¹⁵ for each are:

<table>
<thead>
<tr>
<th>Muscle group</th>
<th>Recommended maximum volumes of fluid for each muscle group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsogluteal (buttocks)</td>
<td>4ml</td>
</tr>
<tr>
<td>Deltoid (upper arm)</td>
<td>1ml</td>
</tr>
<tr>
<td>Vastus lateralis (thigh)</td>
<td>5ml</td>
</tr>
<tr>
<td>Ventrogluteal (hip)</td>
<td>2.5ml</td>
</tr>
</tbody>
</table>

BAP have also published guidelines for preconception, in pregnancy and postpartum¹⁴. They describe how restraint procedures should be adapted to avoid possible harm to the foetus and mother. This will mean that the woman must not be laid supine (risk of obstruction to major blood vessels) or prone (risk to foetus). Any unit that has a pregnant woman admitted should have large beanbags available so that the woman can be lowered into the beanbag and therefore retain a semi-seated position where she is supported. As the
patient will be sitting, and is neither lying supine nor prone, careful consideration must be given to the choice of administration site of any intramuscular injection.

8.0 PRE-TREATMENT CHECKS

8.1 Before prescribing medication for treatment of acutely disturbed behaviour, the prescriber should:

- scrutinise the patient’s notes with regard to his/her general medical history and consider the possibility of carrying out a physical examination
- check for recent ECG*, U&Es and urine drug screen results, previous history of severe extrapyramidal effects, previous response to treatment of acutely disturbed behaviour or other methods of managing imminent violence.
- Review current prescribed medication regimen and check for any recently administered doses of regular and PRN medication.

8.2 Every effort should be made to obtain baseline measurements of temperature, blood pressure, pulse rate, respiratory rate and the level of consciousness prior to the administration of drugs.

9.0 ADDITIONAL FACTORS TO CONSIDER WHEN PRESCRIBING

9.1 Those patients undergoing treatment of acutely disturbed behaviour who are heavily sedated or suspected of using illicit drugs or alcohol should not be secluded. There may be exceptional circumstances were this is necessary, in which case an increased level of observations must be maintained because of the risk of collapse and sudden death. This should comply with level 3 (maintaining the patient within eyesight) of the Trust’s Policy on Engagement and Supportive Observation, CLP8.

9.2 If seclusion is used in other patients the potential complications of treatment of acutely disturbed behaviour should be taken particularly seriously. Level 3 observations must be maintained by a qualified nurse at least until clinical monitoring of the patient’s vital signs is possible.

9.3 Lower doses may be required if alcohol/drug abuse is suspected, or if the patient is antipsychotic naive†.

9.4 If the patient has recently used illicit benzodiazepines, or already receives regular benzodiazepines, an antipsychotic should be used alone.

9.5 If the patient is established on antipsychotics, lorazepam may be used alone.

* The SPC for haloperidol recommends that an ECG should be performed prior to administration, although it is recognised that this may not be feasible if the patient is very disturbed. Ideally, an ECG should be obtained for all patients as soon as possible after admission (to check for QTc prolongation), in case treatment of acutely disturbed behaviour subsequently needs to be used.

† i.e. someone who has never been treated with antipsychotic drugs.
9.6 Caution should be used if the patient is receiving regular antipsychotics, antidepressants or lithium, as drug combinations may increase CNS toxicity.

9.7 The maximum dose of olanzapine is 20mg/24 hours by any (combined) route(s). This should not be exceeded. Not more than 3 IM doses are to be given in any 24-hour period, for up to 3 days. Wait 2 hours between each IM dose.

9.8 Caution should be used with antipsychotics in young male patients as they are prone to dystonia reactions. Procyclidine should be considered.

9.9 Older patients (>65 years) should normally be commenced on no more than half of the recommended adult doses, and special care is required. Frailty should be taken into consideration.

9.10 In dementia, haloperidol is licensed for the treatment of persistent aggression and psychotic symptoms in patients with moderate to severe Alzheimer's dementia and vascular dementia when non-pharmacological treatments have failed and when there is a risk of harm to self or others. Risperidone is indicated for the short-term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others.

Lorazepam and promethazine can both worsen confusion, and doses should be kept to a minimum.

9.11 Lower doses may be needed in patients with learning disabilities. Evidence is limited and extrapolated. Particular consideration needs to be given to the higher susceptibility of patients with learning disability to side effects, and the potential for paradoxical reactions to benzodiazepines.

9.12 If a woman with bipolar disorder develops severe manic or psychotic symptoms and behavioural disturbance during pregnancy or the intrapartum period treatment of acutely disturbed behaviour with an antipsychotic should be considered in preference to a benzodiazepine. If an antipsychotic is used, it should be at the minimum effective dose because of neonatal extrapyramidal symptoms; if a benzodiazepine is use, the risks of floppy baby syndrome should be taken into account. During the perinatal period treatment should be in collaboration with an anaesthetist and/or paediatrician.\(^5\),\(^6\)

9.13 Severe behavioural disturbance in children and adolescents with bipolar disorder should be managed as for adults except that treatment of acutely disturbed behaviour with haloperidol is not recommended because of the increased risk of extrapyramidal side effects in this age group.\(^5\)

9.14 Risperidone, olanzapine and aripiprazole are available as orodispersible formulations which may be easier for some patients to take and more difficult to spit out.\(^5\) The orodispersible formulations of these drugs are not more rapidly absorbed than conventional tablets, but they do render covert non-adherence more difficult.
9.15 Drugs, particularly in the context of restraint, should be used with caution because of the risk of:

- loss of consciousness
- loss of airway
- over-sedation with loss of alertness
- cardiovascular and respiratory complications and collapse
- seizures
- interactions with medicines already prescribed or illicit substances
- akathisia which can worsen aggression
- possible damage to the therapeutic relationship between patient and clinician
- specific issues relating to diagnosis and physical conditions

9.16 Antipsychotics are best avoided in those with cardiovascular disease. Potent ‘typical’ antipsychotics such as haloperidol are best avoided in patients who are antipsychotic naïve or have a history of severe extrapyramidal side effects. Benzodiazepines are best avoided in those with compromised respiratory function.

9.17 Suitable drugs for treatment of acutely disturbed behaviour need to have a rapid onset of action. Frequent small doses are safer and more effective than a single large dose, but this may lead to a risk of accumulation. Therefore the drugs used should have a short duration of action. Previous medication taken and the pharmacokinetics of the agents used should be considered (e.g. time to peak plasma level).

9.18 Where possible, use of a single agent is preferred to a combination. Two drugs of the same class should not be used for the purpose of rapid tranquillisation.

Concomitant use of two or more antipsychotics should be avoided on the basis of risk associated with QT prolongation (common to almost all antipsychotics). This is particularly important where the patient’s history or physical state indicates higher risk of cardiac arrhythmia.

9.19 When using IM haloperidol (or any other ‘typical’ antipsychotics) as a means of managing disturbed/violent behaviour, an antimuscarinic agent, such as procyclidine should be immediately available and should be given orally, intramuscularly in line with the manufacturer’s instructions.

9.20 Sufficient time should be allowed for a clinical response to occur between IM doses of medication.

9.21 Clinicians need to understand the cardio-respiratory effects of the acute administration of drugs used in treatment of acutely disturbed behaviour and the need to titrate dosage to effect. There is a risk of respiratory depression when benzodiazepines are given in high doses or in combination with other hypno-sedatives, including alcohol and some illicit drugs.
9.22 Violent behaviour can be managed without prescribing unusually high doses, of drugs. The minimum effective dose should be used and the British National Formulary\(^8\) (BNF) and BNF for Children\(^9\) recommendations for maximum doses should be adhered to unless exceptional circumstances arise.\(^4\)

9.23 When IM lorazepam is unavailable IM promethazine is recommended as the first line alternative for monotherapy.

### 10.0 CLINICAL MONITORING OF VITAL SIGNS

10.1 Patients who have received drug treatment for acutely disturbed behaviour must not be left unattended. Close monitoring and recording of vital signs by nursing staff is necessary to ensure prompt recognition of serious complications. Monitoring of vital signs must be recorded using the MEWS Form and filed in the patient’s healthcare record.

The BAP guidelines\(^10\) include recommendations for physical health monitoring, and psychiatric monitoring, following the use of pre-RT and after RT, see table below.

<table>
<thead>
<tr>
<th>Level</th>
<th>Criteria</th>
<th>Physical monitoring schedule</th>
<th>Minimum psychiatric observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Pre-RT</td>
<td>MEWS every hour for minimum 1 hour</td>
<td>Standard psychiatric observations every hour</td>
</tr>
<tr>
<td>Medium</td>
<td>All patients post IM RT, who do not require high/critical level monitoring</td>
<td>MEWS every 15 minutes for minimum 1 hour</td>
<td>Intermittent psychiatric observations every 15 minutes</td>
</tr>
<tr>
<td>High</td>
<td>All patients post IM RT, who are over-sedated, asleep, or significantly physically unwell</td>
<td>MEWS every 15 minutes for minimum 1 hour and include pulse oximetry until patient is ambulatory</td>
<td>Continuous (within line of sight)</td>
</tr>
<tr>
<td>Critical</td>
<td>All patients post IV RT as well as patients who are unconscious (not rousable) or severely physically unwell</td>
<td>Continuous monitoring and resuscitation facilities are essential</td>
<td>Continuous (within arm’s length)</td>
</tr>
</tbody>
</table>

10.2 Level of consciousness, blood pressure, pulse, temperature, respiratory rate, oxygen saturation (pulse oximetry), (or if not available any change in skin colour which indicates cyanosis) should be recorded at regular intervals (see
below). The patient’s level of hydration should also be assessed if possible; otherwise physical observation of drinking quantity. *The patient should be encouraged to drink water to maintain adequate hydration.*

**Non-contact physical monitoring**

Physical health monitoring essentially requires direct ‘hands-on contact’ but also needs to be practically feasible and safe. There will be times when direct contact physical observations are associated with increased risks to staff and/or the patient and may even have the counterproductive effect of re-escalating a situation. Examples may involve a secluded patient or one whose degree of acute disturbance is associated with poor engagement with clinicians. For this difficult-to-monitor patient group, there is no evidence base or guidance as to what may constitute non-contact physical monitoring. Respiratory rate, level of consciousness and clinical observational signs (pallor, signs of pyrexia, evidence of dystonia or akathisia and signs of dehydration) have been suggested as practical for such scenarios until direct contact physical monitoring can be established. Therefore the latest version of MEWS chart includes prompts for the observer to record these non-contact observations, using a set of predefined codes, rather than just recording “refusal”. Remote monitoring devices and non-contact monitoring equipment may improve rates of monitoring.

10.3 The importance of maintaining an unobstructed airway, and nursing in the recovery position if necessary should be recognised. 

10.4 Observations should be particularly frequent when a patient is sedated or if IM or IV injections have been administered.

<table>
<thead>
<tr>
<th>Physical monitoring recommendations following RT (parenteral treatment of acutely disturbed behaviour)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For the FIRST HOUR after the last parenteral drug administration:</strong></td>
<td></td>
</tr>
<tr>
<td>- Alertness (AVPU score)</td>
<td>Every 5 minutes</td>
</tr>
<tr>
<td>- Pulse</td>
<td></td>
</tr>
<tr>
<td>- Respiratory rate</td>
<td></td>
</tr>
<tr>
<td>- Blood pressure</td>
<td></td>
</tr>
<tr>
<td>- Temperature</td>
<td></td>
</tr>
<tr>
<td>- Level of hydration if available (otherwise visual obs of drinking quantity)</td>
<td>Every 10 minutes</td>
</tr>
<tr>
<td>- Oxygen saturation (if available)(otherwise assessment of skin colour for cyanosis)</td>
<td></td>
</tr>
<tr>
<td>- Side effects (akathisia/ dystonia)</td>
<td></td>
</tr>
</tbody>
</table>
After the first hour after the last parenteral drug administration for at least the next three hours and until the patient is ambulatory:

- Alertness (AVPU score)
- Pulse
- Respiratory rate
- Blood pressure
- Temperature
- Level of hydration if available (otherwise visual obs of drinking quantity)
- Oxygen saturation (if available) (otherwise assessment of skin colour for cyanosis)
- Side effects (akathisia/ dystonia)

Every 30 minutes

Once the patient is ambulatory:

- Continue to monitor alertness, mental state and behaviour for 6 hours
- Re-start physical observations if there are any concerns

Definitions

Akathisia: Subjective feelings of inner tension and restlessness, with a desire to move. Objective evidence of restlessness, including moving the limbs, shifting the feet, altering the body position when sitting, moving the body weight from one foot to the other when standing, walking on the spot, and pacing about.

Dystonia: a movement disorder characterized by sustained muscle contractions which cause twisting and repetitive movements or abnormal postures.

10.5 ECG and haematological monitoring are also strongly recommended when parenteral antipsychotics are given, especially when higher doses have been used. Hypokalaemia, stress and agitation place the patient at risk of cardiac arrhythmias.

10.6 If the patient appears to be or is asleep, or verbal responsiveness is lost, more intensive monitoring is required, identical to that needed following general anaesthesia. The use of pulse oximetry to continuously monitor oxygen saturation is desirable, and a nurse should remain with the patient until ambulatory. The same should occur where intravenous administration has taken place, BNF limits exceeded, where the patient has used alcohol or illicit drugs and has a relevant medical disorder or concurrently take other medication.4

10.7 Where any irregularities in vital signs are identified, immediate medical assistance should be sought.

10.8 Some observations may not be possible if the patient remains agitated or aggressive or refuses to co-operate. Visual observations must be maintained including respiratory rate and skin colour in these circumstances.
11.0 ENTRIES INTO CLINICAL NOTES

11.1 Medical Staff

11.1.1 When medicines are first prescribed for treatment of acutely disturbed behaviour (either as PRN in anticipation of disturbed behaviour, or at the time of an event) the doctor should take into consideration:

- review of general medical history
- review of ECG, physical investigations if possible
- physical examination (or reason why not possible)
- previous response to drugs used for treatment of acutely disturbed behaviour and any adverse effects
- assessment of potential for illicit drug/alcohol use
- review of current prescribed medications
- the frequency of physical monitoring agreed with the clinical/nursing team
- whether the choice of medicines is covered by an advance statement

11.1.2 When parenteral medicines are prescribed for the management of acutely disturbed behaviour, the medical notes should make reference to the circumstances that may necessitate the use of parenteral administration rather than oral, e.g. the patient refuses oral medication.

11.2 Nursing Staff

11.2.1 A full written account of the incident must be made as soon as possible, in the nursing notes detailing why treatment of acutely disturbed behaviour was necessary. This should include:

- the nature of acutely disturbed behaviour – precipitants, victim, weapon, severity etc
- the time course of events from the onset of the behaviour until the offering of oral medication
- the impact of non-drug strategies, including the timing
- the acceptance or refusal of oral medication
- the name, formulation and dose of medicine given, (including route and muscle site if intramuscular, and the nature of any restraint in place during injection, e.g. prone/supine/sitting)
- the time the medicine dose was given, and the time of any repeated doses
- the impact of the administration of medication
details of all physical observations as agreed with the clinical team.

• subsequent revisions to the management plan

<table>
<thead>
<tr>
<th>12.0 AFTER THE TREATMENT OR ACUTELY DISTURBED BEHAVIOUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.1 The patient should be reintegrated into the ward environment as soon as it is safe to do so.</td>
</tr>
<tr>
<td>12.2 All patients should be offered the opportunity to discuss their experiences as soon as possible after the event and ideally within 72 hours. They should be provided with a clear explanation of the decision to use treatment of acutely disturbed behaviour.</td>
</tr>
<tr>
<td>12.3 The post-incident review should address what happened during the incident, any trigger factors, each person’s role in the incident, how they felt during the incident, how they feel at the time of the review, how they may feel in the near future, and what can be done to address their concerns.</td>
</tr>
<tr>
<td>12.4 If possible, a person not directly involved in the incident should lead the review. The review should be documented in the patient’s notes.</td>
</tr>
<tr>
<td>12.5 As a minimum a doctor and a nurse should be involved in a ‘debrief’ after an episode of RT (POMH-UK standard).</td>
</tr>
<tr>
<td>12.6 They should be given an opportunity to write their account of the experience in their notes.</td>
</tr>
<tr>
<td>12.7 Following an incident the person in charge at the time, or unit co-ordinator, with the support of a consultant practitioner/risk management team will ensure that the requirements of Trust policies CP3 (Adverse Incidents Policy) and CLP28 (Clinical Risk Assessment and Management) are met.</td>
</tr>
<tr>
<td>12.8 This should include:</td>
</tr>
<tr>
<td>• diffusing / debriefing (formal/informal as appropriate)</td>
</tr>
<tr>
<td>• a multidisciplinary clinical case and care plan review and audit</td>
</tr>
<tr>
<td>• completion of Datix form including a copy of the completed Physical Monitoring Form</td>
</tr>
<tr>
<td>• review observation status</td>
</tr>
<tr>
<td>• consideration must be given to nursing within a more secure environment e.g. transfer to PICU</td>
</tr>
<tr>
<td>• further investigation if necessary</td>
</tr>
</tbody>
</table>
13.0 REMEDIAL MEASURES

13.1 The administration of treatment of acutely disturbed behaviour is not without the risk of resulting adverse effects.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Remedial Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute dystonia (including oculogyric crises)</td>
<td>Give procyclidine 5-10 mg IM</td>
</tr>
<tr>
<td></td>
<td>Procyclidine 1.25-2.5 mg in children</td>
</tr>
<tr>
<td>Reduced respiratory rate (&lt;10/minute)</td>
<td>Given oxygen; raise legs; ensure patient is not lying face down</td>
</tr>
<tr>
<td>Reduced respiratory rate (&lt;10/minute)</td>
<td>Give flumazenil if benzodiazepine-induced respiratory depression suspected (see section 13)</td>
</tr>
<tr>
<td>or oxygen saturation &lt;90%</td>
<td>If induced by any other sedative agent ventilate mechanically</td>
</tr>
<tr>
<td>Irregular or slow pulse (&lt;50/minute)</td>
<td>Refer to specialist medical care immediately</td>
</tr>
<tr>
<td>Fall in blood pressure (&gt;30mmHg orthostatic drop or &lt;50mmHg diastolic)</td>
<td>Lie patient flat; tilt bed towards head. Monitor closely</td>
</tr>
<tr>
<td>Increased temperature</td>
<td>Withhold antipsychotics (Risk of NMS and arrhythmias. Check creatinine kinase levels urgently)</td>
</tr>
</tbody>
</table>

14.0 USE OF FLUMAZENIL FOR BENZODIAZEPINE REVERSAL

14.1 Flumazenil is a specific reversal agent for benzodiazepine-induced respiratory depression. It is held at all sites where injectable lorazepam is stocked.

<table>
<thead>
<tr>
<th>Indications for use</th>
<th>If the respiratory rate falls below 10/minute after the administration of lorazepam (diazepam or midazolam)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contra-indications</td>
<td>Patients with epilepsy who have been receiving long-term benzodiazepines</td>
</tr>
<tr>
<td>Caution</td>
<td>Dose should be carefully titrated in hepatic impairment</td>
</tr>
<tr>
<td>Dose and route of administration</td>
<td>Initially 200 mcg intravenously* over 15 seconds (10 mcg/kg max single dose 200 mcg in children under 12 years)</td>
</tr>
<tr>
<td></td>
<td>If the required level of consciousness is not achieved after 60 seconds then subsequent dose: 100 mcg intravenously over 10 seconds</td>
</tr>
</tbody>
</table>
* IV injection of flumazenil must be given by a doctor.

<table>
<thead>
<tr>
<th>Time before dose can be repeated</th>
<th>60 seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Further doses of 100 mcg can be repeated at 60 second intervals where necessary to a maximum of 1 mg</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maximum dose</th>
<th>1 mg in 24 hours (one initial dose and eight subsequent doses)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Patients may become agitated, anxious or fearful on awakening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Seizures may occur in regular benzodiazepine users</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Management</th>
<th>Side effects usually subside</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>• What to monitor?</td>
</tr>
<tr>
<td>• How often?</td>
</tr>
<tr>
<td>Note: if respiratory rate does not return to normal or patient is not alert after initial doses given then assume sedation due to some other cause.</td>
</tr>
</tbody>
</table>

**15.0 USE OF ZUCLOPENTHIXOL ACETATE (CLOPIXOL ACUPHASE®)**

15.1 Zuclopenthixol acetate (Clopixol Acuphase®) is not an appropriate drug for use in rapid tranquillisation, although it is used in the pharmacological treatment of acute psychosis. It has a significantly delayed onset of action and a relatively long duration of action.

15.2 It may have a role in the ongoing management of a risk of violence once tranquillisation has been satisfactorily achieved, and should only be used after an acutely psychotic patient has required repeated injections of short achieving antipsychotic drugs such as haloperidol and olanzapine, or sedative drugs such as lorazepam.

15.3 It is important to consider the pharmacokinetics of other drugs when prescribing it. For example, caution is necessary in a patient who has recently received a dose of a depot antipsychotic which has not yet reached peak levels.
15.4 Acuphase should only be given when enough time has elapsed to assess the full response of previously injected drugs. Consideration should be given to leaving at least 15 minutes after IV injections and 60 minutes after IM injections.

15.5 Acuphase should never be administered:
- in an attempt to ‘hasten’ the antipsychotic effect of any other antipsychotic therapy
- for rapid tranquilisation (onset of effect is too slow), unless judged necessary
- at the same time as other parenteral antipsychotics or benzodiazepines (may lead to oversedation)
- at the same time as depot medication
- as a ‘test dose’ for zuclopenthixol decanoate depot
- to patients who accept a regimen of oral medication that will mitigate their presentation
- to a patient who is unconscious
- to a patient who is physically resistive (risk of intravasation and oil embolus)
- to those with cardiac disease, hepatic or renal impairment or in pregnancy or under 12 years old
- to those who are sensitive to extrapyramidal side effects
- to those who the neuroleptic-naive

15.6 Doses of 50-150mg may be given up to a maximum of 400mg over a two week period, with at least 24 hours between doses. There is no such thing as a ‘course of Acuphase’ and the patient should be assessed before each administration. The maximum dose per 2 weeks is intended to allow a treatment plan to be put in place and does not indicate that there are known harmful effects from more prolonged use. However, such use would be exceptional.

15.7 Sedative effects usually begin to be seen 2 - 4 hours after injection. Peak plasma concentrations occur after 36 hours. At 72 hours, plasma concentrations are around a third of those at 36 hours.

A significant reduction in psychosis is first evident only after 8 hours. The usefulness is therefore limited by a somewhat delayed onset of both sedation and antipsychotic actions. If given to a restrained patient, their behaviour on release from restraint is likely to be unchanged, and will remain as such for several hours.

15.8 The BNF advises obtaining an ECG prior to the use of zuclopenthixol acetate.
16.0 AIMS

16.1 To manage an agitated, hostile or violent episode using a pharmacological approach which is safe for the patient and alleviate disturbing symptoms.

16.2 To achieve a state of calm sufficient to minimise the risk posed to the patient or to others, and to allow the service user to participate in further assessment and treatment.

16.3 To use the lowest effective dose(s) of medication and provide the lowest possibly side-effect load.

The patient should be able to respond to communication throughout the episode of treatment. Deep sedation/sleep is not a desirable endpoint. A state of calm is preferred, with the patient remaining conscious where possible.

17.0 RESPONSIBILITIES

17.1 It is the responsibility of Clinical Directors to ensure that medical staff are aware of this clinical guideline and have received training in the implementation of the pharmacological management of acutely disturbed behaviour. It is the responsibility of Clinical Directors to ensure that medical staff receive training in immediate life support (see CLP14).

17.2 There is a drive internationally to reduce restrictive practices. In the UK, there is a government directive to reduce all forms of restrictive practices, with an objective of ending the use of prone (face-down) restraint; restrictive practices should only be used as a last resort in emergency situations. There is also a focus on corporate responsibility; each Trust Board should be fully informed of the position of their Trust on restrictive practices and the management plan to reduce their use, should identify an Executive Director to lead on recovery approaches and reducing restrictive practices, and should publish an annual report on its use of restrictive interventions.

17.3 It is the responsibility of Ward Managers/Charge Nurses on all in-patient units to ensure that registered nursing staff (both permanent and temporary) are aware of this clinical guideline and have received training in its implementation.

17.4 It is the responsibility of Ward Managers/Charge Nurses to ensure that the correct equipment for resuscitation is monitored on a weekly basis and that this monitoring is documented. It is the responsibility of Ward Managers/Charge Nurses to ensure that nursing staff receive training in immediate life support (see CLP14).

17.5 It is the responsibility of the Head of Workforce Development and Training to ensure that training on the pharmacological management of acutely disturbed behaviour and immediate life support is provided for Trust staff.

17.6 It is the responsibility of the Clinical Audit Manager to ensure that quality assurance arrangements are in place to measure clinical performance annually.
Each **individual qualified practitioner**, together with the ward manager/charge nurse is responsible for ensuring that the appropriate procedures are followed and that the use of treatment for the pharmacological management of acutely disturbed behaviour is documented in line with the requirements of the procedural guideline.

### 18.0 IMPLEMENTATION

18.1 This clinical guideline will be made available across the organisation via the Trust intranet.

18.2 All incidents of acutely disturbed behaviour must be reported in line with Trust policy CP3 on adverse incidents including Serious Untoward Incidents (SUIs).

### 19.0 PHARMACOLOGICAL AGENTS

19.1 Detailed guidance on the drugs used in the management of acutely disturbed behaviour can be found in the relevant sections of the Trust’s Formulary and Prescribing Guidelines.

### 20.0 TRAINING

20.1 Staff who come into contact with patients must appreciate the complexities of human behaviour regarding the management of violence and aggression, including precipitating and trigger factors.¹

20.2 Training in the use and dangers of treatment of acutely disturbed behaviour is as essential as training in de-escalation and restraint. Health professionals should be as familiar with the properties of benzodiazepines as they are with those of antipsychotics.⁴

20.3 Doctors and qualified nurses who use treatment of acutely disturbed behaviour should be trained in the assessment and management of service users in this context, including the risk of these drugs, prescribing within therapeutic limits, the use of flumazenil and techniques and equipment for cardio-pulmonary resuscitation.⁴

20.4 Specifically they should:

- be able to assess the risks associated with treatment of acutely disturbed behaviour, particularly when the patient is highly aroused, may be misusing drugs or alcohol, be dehydrated, or possibly be physically ill
- understand the cardio-respiratory effects of the acute administration of these drugs and the need to titrate dosage to effect
- recognise the important of nursing in the recovery position, patients who receive these drugs and also of monitoring pulse, blood pressure and respiration, and reporting concerns to the person in charge
- undertake annual re-training in cardio-pulmonary resuscitation techniques in line with Trust policy CLP14.
- understand the importance of maintaining an unobstructed airway
A training needs analysis has been undertaken to identify which staff require what level of training to ensure the needs outlined above are met. All qualified staff in areas where treatment of acutely disturbed behaviour is undertaken are expected to undertake training relevant to its use as part of their mandatory and core practice training. This includes:

- Prevention and Management of Violence and Aggression
- Cardio-Pulmonary Resuscitation
- Enhanced Clinical Care
- Medicines Management

This section should be read in conjunction with the following policies:

- HR21 Induction/Mandatory Training Policy
- RM05 Restrictive Practice Policy
- CLP14 Policy for Cardio-Pulmonary Resuscitation
- CLP13 Policy for the Safe and Secure Handling of Medicines

The Workforce Development and Training Department will report monthly on compliance levels for mandatory training for the Executive Team, Workforce and Business Support Service Board and Health, Safety and Security Committees.

Service managers and Directors will be able to check training compliance through the training tracker via the Trust Intranet.

Staff who are booked onto mandatory / core practice training and are, for whatever reason, unable to attend, MUST inform their relevant Director of their reasons.

Staff who do not attend a Mandatory or Core Practice course will receive notification from the Information Department informing them of their non-attendance. Managers will receive a copy of this. From this information non-attendees will be automatically re-booked onto another course by the Information Department. If an individual fails to attend on the second occasion, the service Director will be notified.

If an individual fails to attend on the second occasion, the service Director will be notified and the conduct procedures will be initiated if appropriate.

The Director of Clinical Governance and Quality will be responsible for the overall monitoring and review of this clinical guideline.

This clinical guideline will be reviewed every three years taking into account emerging national guidance, local audit recommendations and lessons learnt from reports, inquiries and positive practice initiatives.
21.3 Any amendments to this clinical guideline will be submitted for consideration and endorsement prior to being ratified to:

- Medicines Management Group
- Clinical Governance & Quality Committee
- PMVA Lead Trainer
- Operational Service Management Group

21.4 Effectiveness of this clinical guideline will be monitored through the Trust Clinical Governance department. The Trust Clinical Governance Department will co-ordinate an annual audit of rapid tranquillisation procedures for the pharmacological management of acutely disturbed behaviour, which will include as a minimum the audit of prescribing and monitoring (including documenting) of service users following treatment for the pharmacological management of acutely disturbed behaviour. The results will be presented to Clinical Advisory Group (CAG) for review and identification of any actions required.

21.5 Training requirements will be monitored by the Workforce, Development and Training Department.

### 22.0 REFERENCES


ANNEXES

Annex 1

Effects of antipsychotics on QTc

<table>
<thead>
<tr>
<th>No effect</th>
<th>Low effect</th>
<th>Moderate effect</th>
<th>High effect</th>
<th>Unknown effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brexpiprazole</td>
<td>Aripiprazole</td>
<td>Amisulpride</td>
<td>Any intravenous antipsychotic</td>
<td></td>
</tr>
<tr>
<td>Cariprazine</td>
<td>Asenapine</td>
<td>Chlorpromazine</td>
<td>Pimozide</td>
<td></td>
</tr>
<tr>
<td>Lurasidone</td>
<td>Clozapine</td>
<td>Haloperidol</td>
<td>Sertindole</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flupentixol</td>
<td>Iloperidone</td>
<td>Any drug or combination of drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluphenazine</td>
<td>Levomepromazine</td>
<td>used in doses exceeding</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Loxapine</td>
<td>Melperone</td>
<td>recommended</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Perphenazine</td>
<td>Quetiapine</td>
<td>maximum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prochlorperazine</td>
<td>Ziprasidone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Olanzapine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paliperidone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Risperidone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sulpiride</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

See original table in Maudsley for full details of individual risks.

Cautions for haloperidol

Haloperidol is contraindicated in combination with medicinal products known to prolong the QTc interval. Examples include:

• Class IA antiarrhythmics (e.g. disopyramide, quinidine).
• Class III antiarrhythmics (e.g. amiodarone, dofetilide, dronedarone, ibutilide, sotalol).
• Certain antidepressants (e.g. citalopram, escitalopram).
• Certain antibiotics (e.g. azithromycin, clarithromycin, erythromycin, levofloxacin, moxifloxacin, telithromycin).
• Other antipsychotics (e.g. phenothiazine derivatives, sertindole, pimozide, ziprasidone)
• Certain antifungals (e.g. pentamidine).
• Certain antimalarials (e.g. halofantrine).
• Certain gastrointestinal medicinal products (e.g. dolasetron).
• Certain medicinal products used in cancer (e.g. toremifene, vandetanib).
• Certain other medicinal products (e.g. bepridil, methadone).
This list is not exhaustive.

Caution is advised when haloperidol is used in combination with medicinal products known to cause electrolyte imbalance. Electrolyte disturbances such as hypokalaemia and hypomagnesaemia increase the risk for ventricular arrhythmias and must be corrected before treatment with haloperidol is started. Therefore, baseline and periodic electrolyte monitoring is recommended.

**Effect of promethazine on QTc**

Promethazine induces significant QTc prolongation in people without cardiovascular disorders, but the lack of simultaneous changes in transmural dispersion of repolarisation (TDR) makes the risk of its torsadogenic action very low. Among many drugs that prolong ventricular repolarisation, only a subset of them is able to provoke torsade de pointes (TdP). This originates from the fact that induction of QT lengthening must be accompanied by a parallel increase in TDR to promote torsadogenesis. Since most QT prolonging drugs, including promethazine, are not able to provoke a simultaneous increase in TDR, the number of drugs that induce TdP is fortunately low.  

---

16
Annex 2

Recommendations on injection site for common IM drugs.

<table>
<thead>
<tr>
<th>Drug</th>
<th>BNF</th>
<th>SPC</th>
<th>Maudsley’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam IM</td>
<td>By intramuscular injection, no site specified</td>
<td>Ativan 4mg/ml Injection, Pfizer IM, no site specified</td>
<td>“Can be administered in gluteal, deltoid or frontal thigh area, according to manufacturer”.</td>
</tr>
<tr>
<td>Promethazine IM</td>
<td>By deep intramuscular injection, no site specified</td>
<td>Phenergan 25mg/ml Injection, Aventis Deep IM, no site specified, perform carefully to avoid inadvertent SC which can lead to local necrosis</td>
<td>Deep IM. Can be administered into thigh, upper arm, or gluteal. Ensure muscle mass is sufficient for the volume being injected.</td>
</tr>
<tr>
<td>Haloperidol IM</td>
<td>By intramuscular injection, no site specified</td>
<td>Haloperidol 5mg/ml Injection, Mercury IM, no site specified</td>
<td>Preferably, select gluteal when dose volume high. Deltoid preferred for low doses. There is no information on dose limits for specific muscle groups; choice is at discretion of prescriber.</td>
</tr>
<tr>
<td>Olanzapine IM</td>
<td>By intramuscular injection</td>
<td>Zyprexa 10mg Injection, Eli Lilly IM, no site specified</td>
<td>Inject slowly, deep into muscle. Exact site not specified, choice is a clinical decision.</td>
</tr>
<tr>
<td>Aripiprazole IM</td>
<td>By intramuscular injection</td>
<td>Abilify 7.5mg/ml Injection, Otsuka IM. Injection into deltoid or deep into gluteus is recommended.</td>
<td>As per SPC. Avoid adipose regions.</td>
</tr>
</tbody>
</table>

SPC: Summary of product characteristics.