Grampian Staff Guidance For Rapid Tranquillisation For Use In The Adult In-Patient Setting

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Executive Sign-Off
This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature:  

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Purpose / description: This guidance has been developed to ensure that in psychiatric emergencies all adult in-patients requiring rapid tranquillisation, if acutely disturbed or aggressive, receive their medication safely and correctly and that the proper procedures have been followed.

Responsibility: Responsibility for the effective management of this policy ultimately lies with the General Managers for the Acute and Mental Health/Learning Disabilities Sectors. Delegation for formulating, disseminating and controlling these documents falls to either a named individual or a working group.

Policy statement: It is the responsibility of individual healthcare professionals and their line managers to ensure that they work with the terms laid down in this guidance and to ensure that staff are working to the most up to date guidance. By doing so, the
quality of the services offered will be maintained, and the chances of staff making erroneous decisions which may affect patient, staff or visitor safety and comfort will be reduced. Supervisory staff at all levels must ensure that healthcare professionals using this guidance act within their own level of competence.

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Hospital/Interface services: Associate Medical Director and Associate Nurse Director, Mental Health and Learning Disability Services
Operational Management Unit: Clinical Directors, Mental Health and Learning Disability Services and Hosted and Moray Service Managers
Departmental: Line Managers
Area: Line Managers

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Hospital/Interface services: Assistant General Managers and Group Clinical Directors
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Review: This policy will be reviewed in three years or sooner if current treatment recommendations change.

Responsibilities for review of this document:
Lead Author/Coordinator: Principal Pharmacist, Mental Health and Learning Disability Services

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<td>– “Oral medication should be offered...” - “if practicable” added.</td>
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<td>• Haloperidol contraindications. Updated as per current Summary of Product Characteristics (SPC) following EU harmonisation process.</td>
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- Senior Nurse Group Mental Health and Learning Disabilities
- Senior Staff Group, Moray Mental Health Service
- Dr. Craig Brown, Consultant in Emergency Medicine

Updated in line with:
- Comments received from Mental Health Operational Medicines Management Group.


Under Acute dystonia (including oculogyric crisis) ‘consider lower maximum in frail/elderly’ added.

New table added.

New table added.

New table added.

Existing references updated and the following added:
- Joint BAP NAPICU evidence-based consensus guidelines for the clinical management of acute disturbance: De-escalation and rapid tranquillisation for use in the adult in-patient setting.

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NB: This guidance has undergone extensive revision as a result of the EU harmonisation process for haloperidol. Due to the recommendation of a pre-treatment ECG and its contraindication with medicinal products known to prolong the QT interval of an ECG, haloperidol is no longer recommended first line for rapid tranquillisation. It is now reserved for specialist use in combination with either lorazepam or promethazine following a risk: benefit analysis by a senior doctor.

1. Definition Of Rapid Tranquillisation

"Rapid Tranquillisation: The 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". 

2. Scope

This guidance has been developed to:

- Provide staff with advice on the pharmacological management of patients who present with disturbed and/or aggressive behaviour in the context of an established or suspected psychiatric disorder including situations where such behaviour arises as a result of an organic brain disorder or physical condition leading to disordered brain functioning.
- Ensure that all adults requiring rapid tranquillisation, if acutely disturbed or aggressive, receive their medication safely and correctly and that the proper procedures and legal requirements have been followed.

3. General Principles Of Rapid Tranquillisation

- Rapid tranquillisation should only be used when appropriate psychological and behavioural approaches have failed to de-escalate acutely disturbed behaviour and the use of ‘as required’ oral medication is ineffective or not possible. It is essentially a treatment of last resort.
- The aim of drug treatment is to calm the person, and reduce the risk of violence and harm, rather than treat the underlying psychiatric condition. An optimal response would be a reduction in agitation or aggression without sedation, allowing the patient to participate in further assessment and treatment. Ideally the drug treatment should have a rapid onset of action and a low level of side effects.
Patients should only be treated with medicines for rapid tranquillisation after an assessment has established that the risk of not doing so is greater than the risk of acute pharmacological treatment.

Patients should be provided with adequate information about medication used for rapid tranquillisation, on admission, so informed decisions can be made about their care and treatment.

Care and risk management plans should be made in conjunction with the patients and/or carers wherever possible.

Multidisciplinary Teams (MDT) should develop and document an individualised pharmacological strategy for using routine and ‘as required’ medication to calm, relax, tranquillise or sedate patients, who are at risk of violence and aggression as soon as possible after admission to an in-patient psychiatric unit. The MDT should review the strategy and the use of medication at least once a week or more frequently if events are escalating and restrictive interventions are being planned/used.

A post incident review (involving the patient if possible) must take place as soon as possible after the incident and must be recorded on DATIX.

4. Before Contemplating Prescribing Rapid Tranquillisation:

Assess the risk to the patient and others.

Consider causes for disturbed behaviour, including an assessment of the patient’s physical state to determine any possible precipitants, make a diagnosis and treat accordingly.

Consider patient’s medical and psychiatric history including previous response to rapid tranquillisation or other methods of managing imminent violence.

Review currently prescribed medication including any “as required” medication recently administered.

The concomitant use of two or more antipsychotics should be avoided if possible on the basis of risk associated with QT prolongation. This is a particularly important consideration in rapid tranquillisation where the patient’s physical state predisposes them to cardiac arrhythmia.

Assess patient for use of illegal drugs or alcohol.

Consider whether the patient has/lacks capacity and is or can be treated under the provisions of either the Mental Health (Care and Treatment) (Scotland) Act 2003 or Adults with Incapacity (Scotland) Act 2000. See section 6.
• Consider any advance statement the patient may have made or current treatment plan (T2B/T3B) if detained under the Mental Health (Care and Treatment) (Scotland) Act 2003 or Section 47 Certificate if subject to the Adults with Incapacity (Scotland) Act 2000. Efforts should be made to ascertain the existence of a Welfare Attorney or Welfare Guardian. See section 6.

5. **Staff Involved In The Prescribing And Administration Of Rapid Tranquillisation Must Be Adequately Trained In:**

• The recognition and management of violent/disturbed behaviour, including use of psychosocial interventions to avoid or minimise restrictive interventions and de-escalation techniques.

• Knowledge of drugs used, their side effects and risks.

• Cardiopulmonary resuscitation.

• Up to date knowledge of the legislation relating to the prescribing and administration of rapid tranquillisation.

• Skills to undertake a post-incident review.

**NB:** At all times a doctor should be available to quickly attend to an alert by staff members when rapid tranquillisation or other interventions are implemented.

6. **Legislation Relating To Rapid Tranquillisation**

6.1. **Common Law**

In medical and psychiatric emergencies in patients not detained under the Mental Health Act, common law allows treatment to protect a patient’s life and/or the wellbeing of others. No certification is needed beyond the documentation of an accurate description of the actions taken within the patient’s notes. However, any patient who has the capacity to make or withhold consent cannot be given medical treatment without that consent. While the use of common law is acceptable in certain emergency situations, judicious application of the Adults with Incapacity (Scotland) Act 2000 and the Mental Health (Care and Treatment) (Scotland) Act 2003 provide a framework for patients deemed incapable of consent to treatment because of a mental disorder.

6.2. **Adults with Incapacity (Scotland) Act 2000**

Under Section 47 of this Act, a patient who is incapable of making decisions about medical treatment can be given “any procedure or treatment designed to safeguard or promote physical or mental health” without their consent, subject to the principles of the Act. The medical practitioner primarily responsible for the medical treatment of the adult must issue a Section 47 Certificate of Incapacity.
The use of force under the Adults with Incapacity (Scotland) Act 2000.

The Act prohibits the use of force or detention, unless it is immediately necessary and only for so long as is necessary in the circumstances.

The interpretation of this will depend on the particular circumstances of each case, but the principles set out in section 1 of the Act must be applied. So, for example, the degree of force applied must be the minimum necessary. Where an adult shows continued resistance to treatment for mental disorder consideration should be given to making use of the options available under mental health legislation.

6.3. Mental Health (Care and Treatment) (Scotland) Act 2003
(Including the Criminal Procedure (Scotland) Act 1995 as amended by the Mental Health (Care and Treatment)(Scotland) Act 2003).

The Act allows for the administration of medication to treat mental disorder (including acutely disturbed behaviour secondary to delirium and dementia and treatment of overdose) without and/or against the patient’s consent. **It does not allow the treatment of an acute unrelated physical disorder without consent.**

In medical emergencies arising in a detained patient, Section 243 of the Mental Health (Care and Treatment)(Scotland) Act 2003 allows the administration of medical treatment without consent to:

- save the patient’s life
- prevent serious deterioration in the patient’s condition
- alleviate serious suffering on the part of the patient
- prevent the patient behaving violently and/or being a danger to him/herself or others.

If the patient is on an Emergency Detention Certificate (this certificate does not authorise treatment under the Act) a T4 form (Record of notification following urgent medical treatment) should be completed and sent to the Responsible Medical Officer (RMO). This form is a notification of the circumstances where it was necessary as a matter of urgency for medical treatment to be given to a patient subject to detention. This form should be sent to the Mental Welfare Commission by the RMO within 7 days of the treatment being given.

If the patient is within the first 2 months of compulsory treatment under the Mental Health (Care and Treatment) (Scotland) Act 2003 then a T4 form for administration of “as required” medication is not necessary. If the patient is beyond the first 2 months then a T2B form (Certificate of Consent to Treatment) and/or a T3B form (Certificate of the Designated Medical Practitioner) should be in place. The Mental Welfare Commission recommends that “as required” intramuscular medication is not recorded on a T2B form as some degree of restraint is likely during the administration of the medication. If the “as required” medication is listed on the T3B form then a T4 form is not required. If the “as required” medication is not listed on the T3B form then a T4 form should be
completed and sent to the RMO who will send to the Mental Welfare Commission within 7 days of the treatment being given.

The administering doctor should ensure that the patient’s RMO Officer has been informed of the administration of the relevant medication.

Further guidance is available from the Mental Welfare Commission for Scotland. Guidance on the administration of covert medication is available from the Mental Welfare Commission for Scotland and the NHS Grampian Staff Guidance On Covert Administration of Medication (Adult Policy)

Further information is available on the following websites for the Mental Health Act and the Adults with Incapacity Act respectively:

7. Principles Of Drug Treatment
(Refer to accompanying tables and treatment algorithm)

• A risk benefit analysis should be undertaken to determine the appropriate medicine choice and dose for the patient. This should include assessing the precautions to prescribing rapid tranquillisation on an individual patient basis (refer to sections 8 and 9 below for more detailed information).

• Oral medication should be offered, if practicable, before intramuscular (IM) medication.

• Write initial prescription as a single dose and do not repeat until the effect has been reviewed.

• The minimum effective dose should be used. Always give time for the drug to work. (Refer to Table 3 for further information).

• When a behavioural disturbance occurs in a non-psychotic context it is preferable to use lorazepam alone, orally or intramuscular if necessary.

• Ensure it is clearly indicated on the KARDEX if maximum daily dose includes regular medication and any oral/IM medication used “as required”. Ensure the interval between “as required” doses is specified. The maximum daily doses of all prescribed drugs should be carefully observed. If it is necessary to exceed these, the reasons for doing so should be recorded in the case notes. Where the total combined antipsychotic load exceeds 100% of the BNF maximum the NHS Grampian High Dose Antipsychotic Guidance should be followed.

• Vital signs must be monitored after intramuscular administration. (Refer to) Table 1: Rapid Tranquillisation Monitoring

• Mixing medicines in the same syringe is hazardous, constitutes an unlicensed product, and should NEVER be done.
Facilities for resuscitation must be available.

Flumazenil must be available to reverse respiratory depression due to lorazepam.

NB: Flumazenil is administered intravenously. (Refer to Table 2: Side effects of drugs used in rapid tranquillisation and their management). If required flumazenil must be prescribed and administered by a doctor who has knowledge of the prescribing and administration of flumazenil.

Always have an injectable anticholinergic, e.g. procyclidine available to reverse an acute dystonic reaction due to antipsychotic medication (Refer to Table 2).

If rapid tranquillisation is being used, a senior doctor should review all medication at least once a day.

8. Medicines for Rapid Tranquillisation

The following factors should be taken into account when determining drug choice for rapid tranquillisation:
- The patient’s preferences or advance statements and decisions
- Pre-existing physical health problems or pregnancy
- Possible intoxication
- Previous response to medications; including adverse effects
- Potential for interactions with other medications
- The total daily dose of medications prescribed and administered.

NB: For anatomical sites for intramuscular administration see Table 7.

**Lorazepam IM Injection**
- 2mg (500micrograms – 2mg in frail/elderly); repeat after 30 – 60 minutes if required.
- Maximum 6 – 8 mg/24 hours.
- Dilute with an equal volume of water for injection or sodium chloride 0.9% injection.

**Promethazine IM Injection**
- 25 – 50mg (consider lower dose in frail/elderly); repeat after 1 – 2 hours if required.
- Maximum 100mg/24 hours (consider lower maximum in frail/elderly).
- Promethazine may be a useful option, instead of lorazepam, in benzodiazepine tolerant patients. This is an unlicensed use.

**Aripiprazole 7.5mg/mL Short Acting IM Injection (1.3mL)**
- 9.75mg (1.3mL) (consider lower dose 5.25mg (0.7mL) in frail/elderly); repeat after 2 hours if required.
- Maximum 3 injections daily; maximum daily combined oral and parenteral dose 30mg/24 hours.
Dosage adjustments needed if co-prescribed with potent inducers or inhibitors of CYP3A4 or CYP2D6 (see Table 4 and consult product literature).

Licensed for rapid control of agitation and disturbed behaviour in schizophrenia or mania.

Olanzapine 10mg Short Acting IM Injection
- Olanzapine is an alternative short acting IM injection if there are contraindications/intolerance/non-responsiveness to aripiprazole.
- 5 - 10mg (2.5 - 5mg in frail/elderly); repeat after 2 hours.
- Maximum 3 injections daily for 3 days; maximum daily combined oral and parenteral dose 20mg/24 hours.
- When one or more factors present that might result in slower metabolism (e.g. female gender, elderly, non-smoker) consider lower starting dose and more gradual increase).
- Reconstitute with 2.1mL water for injection.
- Do not administer IM lorazepam at the same time as IM olanzapine. When treatment with both IM olanzapine and IM lorazepam is being considered olanzapine must be administered first. If the patient requires IM lorazepam after IM olanzapine, it must not be administered until at least ONE hour after the IM olanzapine and there must be careful monitoring for excessive sedation and cardiorespiratory depression. If the patient has received IM lorazepam, IM olanzapine administration should only be considered after careful evaluation of clinical status and on the advice of a consultant. The patient should be closely monitored.
- Licensed for rapid control of agitation and disturbed behaviour in schizophrenia or mania.

The following IM combination treatments are reserved for specialist use following senior review when other treatment options have failed:

*Haloperidol IM Injection PLUS Lorazepam IM Injection
**NB:** Drugs must not be mixed in same syringe.

*Haloperidol IM Injection PLUS Promethazine IM Injection
**NB:** Drugs must not be mixed in same syringe. This combination is supported by NICE NG10 and the British Association of Psychopharmacology. However following the EU harmonisation process for haloperidol, promethazine is a contraindicated treatment due to the risk of QT prolongation. The decision to use this combination represents an unlicensed use of haloperidol and a risk: benefit analysis must be undertaken by a senior doctor before prescribing and documenting in the clinical notes.

*Note: Haloperidol IM Injection
- Only recommended to be used with either lorazepam IM injection or promethazine IM injection (unlicensed use – see above).
- 5mg (500micrograms – 2mg in frail/elderly); repeat after 30 – 60 minutes if required.
- Maximum 20mg/24 hours (frail/elderly maximum 5mg/24 hours).
The Summary of Product Characteristics (SmPC) indicates that QT prolongation +/or ventricular arrhythmias in addition to sudden death have been reported. The risk increases with dose, in predisposed patients or with parenteral use and the following is highlighted:

- **Pre-treatment ECG recommended.**
- **Contraindicated with medicinal products known to prolong QT interval** (see Table 5 and Table 6).

If haloperidol is to be used without a pre-treatment ECG or with medicinal products known to prolong the QT interval, this constitutes an unlicensed use and poses a risk to the patient. A risk: benefit analysis must be undertaken by a senior doctor before prescribing and documenting in the clinical notes.

**Zuclopenthixol Acetate (Clopixol Acuphase) IM Injection** is not suitable or recommended for rapid tranquillisation due to its delayed onset of action and extended duration of effect. However it may be considered as an option in patients who have required repeated parenteral administration of a short-acting antipsychotic to manage disturbed behaviour. Consult product literature.

### 9. Precautions to Rapid Tranquillisation

- **Patients never previously prescribed antipsychotic medication**
  - Use lower doses.
  - Avoid haloperidol.

- **Patients with no evidence of psychotic symptoms**
  - Use lorazepam.

- **Frail/Elderly**
  - Use lower doses.
  - Caution with promethazine due to anticholinergic side-effects.

- **Organic Disease**
  - Use lower doses.
  - In patients with suspected or confirmed Lewy Body Dementia avoid the use of antipsychotics.
  - Avoid haloperidol in Parkinson’s disease.
  - Caution with aripiprazole in Parkinson’s disease.
  - Avoid antipsychotics in cerebrovascular disease, including vascular dementia.

- **Cardiovascular Disease including Prolonged QT Interval or No ECG**
  - Use lorazepam.
  - Avoid haloperidol.
  - Caution with aripiprazole.
  - Caution with promethazine due to hypotension.
  - Consider any concomitant medication, which may prolong QTc interval.

**NB:** Haloperidol is contraindicated in clinically significant cardiac disorders (bradycardia, QT interval prolongation). A clinical risk assessment must be carried out before prescribing haloperidol.
• Compromised respiratory function
  ➢ Avoid benzodiazepines.
  ➢ Caution with promethazine as may thicken or dry lung secretions and impair expectoration.

• Alcohol Withdrawal/Risk of Seizures
  ➢ Caution when using antipsychotics – lowering of seizure threshold.
  ➢ Caution with promethazine - lowers seizure threshold.

• Hepatic or renal impairment
  ➢ Lower doses may be needed due to reduced clearance. See medicine specific prescribing information.

• Pregnancy
  ➢ Specialist advice must be sought on the management of pregnant women requiring emergency sedation. The risks and benefits of treatment should be considered on a case by case basis.

• Co-morbid Substance Misuse
  ➢ In patients who are benzodiazepine-tolerant consider use of IM promethazine.
  ➢ Care should be exercised if methadone prescribed due to increased potential for QTc prolongation.

10. Consultation

Mental Health Operational Medicines Management Group.
Psychiatric Medical Advisory Committee
Senior Nurse Group Mental Health and Learning Disabilities
Senior Staff Group, Moray Mental Health Service
Dr. Craig Brown, Consultant in Emergency Medicine
**Treatment Algorithm for Rapid Tranquilisation for Use in the Adult In-patient Setting**

The following is for guidance only and may not be appropriate in all circumstances. Discussion with a senior colleague is recommended at any stage.

(This algorithm must only be used in conjunction with accompanying guideline)

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**Step 1 De-escalation**
Assess situation using all information available. Reach working diagnosis taking into account current medication, mental state, drug misuse. Use non-drug measures: talking down, distraction, etc.

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**Step 2 Oral Treatment**
If already on an antipsychotic give Lorazepam 1 - 2mg (500micrograms - 2mg in frail / elderly) or Promethazine 25 – 50mg (consider lower dose in frail/elderly) if benzodiazepine tolerant. Repeat after 45 – 60 minutes.

If not on an antipsychotic an oral antipsychotic is an option:
- Aripiprazole 10mg (lower dose in frail/elderly) OR Quetiapine 50 – 100mg (lower dose in frail / elderly) OR Olanzapine 10mg (2.5 – 5mg in frail / elderly) OR Risperidone 1 - 2mg (500micrograms in frail/elderly). Repeat after 45 - 60 minutes.

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**Step 3 Rapid Tranquilisation (i.e. IM Medication)**
Depending on patient’s preferences/advance statements and decisions; pre-existing physical health problems or pregnancy; possible intoxication; previous response to medications, including adverse effects; potential interactions with other medications; and the total daily dose of medications prescribed and administered:

**EITHER**

LORAZEPAM 2mg IM
(500micrograms - 2mg in frail / elderly)
Maximum IM daily dose usual range 6 – 8mg
Dilute with equal volume of water for injection or 0.9% injection sodium chloride.

OR

^PROMETHAZINE 25 – 50mg IM
(consider lower dose in frail / elderly)
Maximum 100mg/24hours
(consider lower maximum in frail / elderly)

If no response after 30 – 60 minutes (1 - 2 hours for promethazine) repeat above.

If no response after further 30 – 60 minutes (1 - 2 hours for promethazine) seek advice from senior medical staff. Consider need for alternative (refer to guidance p6-8).

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**OR**

^ARIPIPRAZOLE 9.75mg (1.3mL) IM
(consider lower dose 5.25mg (0.7mL) in frail / elderly)
Maximum 3 injections daily
Maximum 30mg/24hours (oral and IM combined)

If no response after 2 hours repeat above.

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**IMPORTANT NOTES**
- Use minimum effective dose.
- In non-psychotic context use lorazepam.
- Lorazepam injection must be diluted with an equal volume of water for injection or sodium chloride 0.9% for injection
- Promethazine is a useful option, instead of lorazepam, in benzodiazepine tolerant patients. NB: unlicensed use.
- *Aripiprazole Short Acting Injection is licensed for rapid control of agitation and disturbed behaviour in schizophrenia and mania. Dosage adjustments needed if co-prescribed with potent inducers or inhibitors of CYP3A4 or CYP2D6 (see Table 4 on p12).
- Include both oral and IM doses when calculating total amount of a drug given. Take regular medication doses into account where relevant.
- In certain circumstances current licensed maximum doses may be knowingly exceeded. The rationale for this should be recorded in the case notes.
- Cardiopulmonary resuscitation equipment must be available.
- Vital signs must be monitored after intramuscular administration (refer to Table 1).
- If respiratory rate falls below 10 per minute due to administration of lorazepam give flumazenil (200micrograms over 15 seconds IV, then if required level of consciousness not achieved after 60 seconds, 100micrograms over 10 seconds, repeated until required level of consciousness achieved to maximum of 1mg). Flumazenil must be prescribed and administered by a doctor who has knowledge of the prescribing and administration of flumazenil.
- Procyclidine 5 - 10mg IM / IV can be given for acute dystonia repeated if necessary after 20 minutes (maximum 20mg daily).
### Table 1: Rapid Tranquillisation Monitoring

**After intramuscular rapid tranquillisation monitor the following:**

At least every hour until there are no further concerns regarding physical health:
- Side-effects
- Pulse
- Blood Pressure
- Respiratory rate
- Temperature
- Level of hydration
- Level of consciousness.

**Increase to monitoring every 15 minutes if:**
- BNF maximum dose exceeded
- Appears asleep or sedated
- Has taken illicit drugs or alcohol
- Has a pre-existing physical health problem
- Has experienced harm as a result of any restrictive intervention.

**NB:**
- If the patient is asleep or unconscious a pulse oximeter should be used to continuously measure oxygen saturation. A nurse should remain with the patient until they are ambulatory again.
- ECG and haematological monitoring are also strongly recommended, especially when higher doses are used. Hypokalaemia, stress, and agitation put the patient at risk of cardiac arrhythmias.
- If olanzapine IM administered pulse and respiratory rate must be monitored for at least 4 hours after administration.
Table 2: Side effects of drugs used in rapid tranquillisation and their management

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute dystonia (Including oculogyric crisis).</td>
<td>Give an anticholinergic, e.g. procyclidine 5 – 10mg (2.5 - 5mg in frail/elderly) IM or IV repeated if necessary after 20 minutes (maximum 20mg/day; consider lower maximum in frail/elderly).</td>
</tr>
</tbody>
</table>
| Reduced respiratory rate (<10/min) or oxygen saturation (<90%) due to administration of lorazepam. | Give oxygen; raise legs; ensure patient is not lying face down.  
  Give flumazenil (a benzodiazepine antagonist) if benzodiazepine-induced respiratory depression suspected.  
  If required flumazenil must be prescribed and administered by a doctor who has knowledge of the prescribing and administration of flumazenil.  
  - Initially 200micrograms IV over 15 seconds, then if required level of consciousness not achieved after 60 seconds, 100micrograms over 10 seconds, repeated until required level of consciousness obtained.  
  - Maximum dose: 1mg (1000micrograms) in 24 hours.  
  - Flumazenil has a shorter half-life than benzodiazepines and respiratory rate may recover then deteriorate again. Monitor patient closely as doses may need to be repeated. |
| Irregular or slow (<50/min) pulse. | Refer to specialist medical care immediately. |
| Fall in blood pressure ( > 30mmHg orthostatic drop or < 50mmHg diastolic). | Lie patient flat, raise legs if possible. Monitor closely. |
| Increased temperature and/or marked rigidity. (Risk of Neuroleptic Malignant Syndrome (NMS) and perhaps arrhythmias). | Withhold antipsychotics.  
  Check creatinine kinase urgently.  
  Monitor closely for any other signs of Neuroleptic Malignant Syndrome (NMS) such as sweating, hypertension, fluctuating blood pressure, tachycardia, urinary incontinence, retention or obstruction, muscle rigidity, confusion, agitation or altered consciousness.  
  If NMS suspected refer to specialist medical care immediately. |
### Table 3: List of medication used for rapid tranquillisation: pharmacokinetics

<table>
<thead>
<tr>
<th>Medication</th>
<th>Time to maximum plasma concentration</th>
<th>Approximate plasma half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole intramuscular injection</td>
<td>1 - 3 hours</td>
<td>75 – 146 hours*</td>
</tr>
<tr>
<td>Haloperidol intramuscular injection</td>
<td>20 - 60 minutes</td>
<td>10 to 36 hours</td>
</tr>
<tr>
<td>Lorazepam intramuscular injection</td>
<td>60 - 90 minutes</td>
<td>12 - 16 hours</td>
</tr>
<tr>
<td>Olanzapine intramuscular injection</td>
<td>15 – 45 minutes</td>
<td>32 – 50 hours</td>
</tr>
<tr>
<td>Promethazine intramuscular injection</td>
<td>1 – 2 hours</td>
<td>7-15 hours</td>
</tr>
</tbody>
</table>

* 75 hours in extensive metabolisers of CYP2D6 and 146 hours in poor metabolisers of CYP2D6.

### Table 4: Strong inhibitors and inducers of CYP2D6 and CYP3A4

(NB: This list is not exhaustive – consult BNF or product literature)

<table>
<thead>
<tr>
<th>Strong inhibitors of CYP2D6</th>
<th>Strong Inhibitors of CYP3A4</th>
<th>Aripiprazole dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>Ketoconazole</td>
<td>Half dose</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Itraconazole</td>
<td></td>
</tr>
<tr>
<td>Quinidine</td>
<td>HIV Protease inhibitors</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5: Antipsychotics and their effect on QTc

<table>
<thead>
<tr>
<th>No Effect</th>
<th>Low Effect</th>
<th>Moderate Effect</th>
<th>High Effect</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Clozapine</td>
<td>Amisulpride</td>
<td>Pimozide</td>
<td>Trifluoperazine</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>Flupentixol</td>
<td>Chlorpromazine</td>
<td></td>
<td>Zuclopenthixol</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Haloperidol</td>
<td></td>
<td>Any intravenous antipsychotic</td>
<td></td>
</tr>
<tr>
<td>Paliperidone</td>
<td>Levomepromazine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>Levomepromazine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulpiride</td>
<td>Any drug or drug combination at more than recommended maximum</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 6: Other medicines that increase QTc
(NB: This list is not exhaustive – consult BNF or product literature)

<table>
<thead>
<tr>
<th>Antidepressants</th>
<th>citalopram, escitalopram, venlafaxine, trazodone, tricyclics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood Stabilisers</td>
<td>lithium</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>ampicillin, azithromycin, erythromycin, clarithromycin, co-</td>
</tr>
<tr>
<td></td>
<td>trimoxazole, ciprofloxacin, levofloxacin, moxifloxacin,</td>
</tr>
<tr>
<td></td>
<td>pentamidine</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>chloroquine, mefloquine, quinine</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>disopyramide, procainamide, sotalol, amiodarone, bretylium,</td>
</tr>
<tr>
<td></td>
<td>quinidine, dronedarone</td>
</tr>
<tr>
<td>Others</td>
<td>methadone (at doses &gt;100mg/day), amantadine, cyclosporin,</td>
</tr>
<tr>
<td></td>
<td>diphenhydramine, hydroxyzine, nicardipine, tamoxifen,</td>
</tr>
<tr>
<td></td>
<td>fluconazole, promethazine</td>
</tr>
</tbody>
</table>

Table 7: Anatomical sites for intramuscular administration

<table>
<thead>
<tr>
<th>Anatomical Site</th>
<th>Deltoid (max volume= 2ml)</th>
<th>Lateral Thigh</th>
<th>Gluteal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole Injection</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Haloperidol Injection</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Lorazepam Injection</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Olanzapine Injection</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Promethazine Injection</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Zuclopenthixol Acetate Injection</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

(Not recommended for rapid tranquillisation)

11. References

1. British National Formulary via Medicines Complete
   https://www.medicinescomplete.com/mc/bnf/current/


7. Joint BAP NAPICU evidence-based consensus guidelines for the clinical management of acute disturbance: De-escalation and rapid tranquillisation 2018
8. Medicines Information Department, Aberdeen Royal Infirmary
9. Medicines Information Department, Otsuka Pharmaceuticals UK Ltd