East London
NHS Foundation Trust

Rapid Tranquillisation of Adults and Older People Policy

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Version	**Date**	**Author**	**Comment**
1.0	October 2012	James Innes	-
2.0	April 2014	Andrea Okoloekwe	Update to section about midazolam: • Absorption erratic and unpredictable • Sedation and respiratory depression may occur more often than with other benzodiazepines • Flumazenil must be available if midazolam is administered.
3.0	August 2014	Andrea Okoloekwe	Maximum dose of haloperidol updated to reflect changes in licensing. Clarification about administration of flumazenil. Maximum dose of intramuscular lorazepam changed.
4.0	June 2016	Jennifer Melville	Remove reference to RT side of prescription chart.
5.0	March 2018	Alan Cottney	**Section 1** (Introduction) added, including reference to updated NICE guideline NG10. Updates and replaces previous section 1 (aims). **Section 2** (Scope) added, and previous section 3 (Principle) removed. Content of previous section 3 incorporated throughout rest of document. Statements about non-pharmacological interventions removed, replaced with signpost to other relevant trust guidance. **Section 3** (Roles and responsibilities): daily prescriber review required if RT is given. Accountability for administration, monitoring and prescription review removed from pharmacist responsibilities. **Section 4** (Terms used in this guideline) added. Previous section 4 (Legal basis) removed, replaced with signpost to relevant trust guidance. **Section 6** (Using p.r.n. medication to prevent violence and aggression) added; incorporating guidance from updated NICE guideline NG10. **Section 7** (Using medication for rapid tranquillisation) added; replacing previous treatment algorithms. Guidance on RT updated in light of NICE NG10; lorazepam on its own or haloperidol+ promethazine now NICE-recommended treatments. Avoid haloperidol if no ECG. Guidance on no/ partial response changed to match NG10. **Section 8** (Specific drug considerations): restructured to incorporate statements from NICE NG10 on medication choice. Aripiprazole added to list of choices for medication. Section on combining drugs added. **Section 9** (intravenous medication): new section. Previous section 6.09 (drug side effects) removed; signpost to BNF & product literature. Previous section 7, 8 and 9 removed; superseded. **Section 10** (Physical health monitoring following rapid tranquillisation) updated to include advice on what to do if observations are in 'amber' or 'red' range. Need to monitor side effects and hydration included. Statement that monitoring forms should be uploaded to RiO & on acceptability of alternative monitoring forms. **Section 11** (Rapid tranquillisation during seclusion) added. **Section 14** (Zuclopenthixol acetate): new section. **Appendix 1**: new treatment tables added. Midazolam dose changed to mcg/kg in line with updated BNF monograph. **Appendix 2**: more information about the cautions and contraindications of flumazenil added. Layout changed. **Appendix 3**: RT monitoring form updated with action to take if amber or red result, hydration and side effects included; pulse, O_2 sats, resp. rate and temperature now stated in range rather than discrete points. **Appendix 4** (source list): new section

6.0	November 2019	Stephanie Tannis-Ellick, Jennifer Melville	Registered Nursing Associates are not permitted to administer rapid tranquillisation, they are permitted to undertake the second check
7.0	May 2020	Simmy Daniel	**Section 14.0**- update on monitoring using an Acuphase monitoring chart **Appendix 5:** Acuphase monitoring chart **Table 1:** Haloperidol IM dose changes updated **References**- updated haloperidol BNF monograph

Contents

1.0 Introduction

1.1 "Rapid tranquillisation" (RT) refers to the use of medication to calm highly agitated individuals in the context of mental disorders who have not responded to non-pharmacological approaches. When RT is used, it is often in the initial stages of the treatment of severe and enduring mental illness.

1.2 The purpose of this document is to provide guidance about the use of parenteral medication for the prevention and management of violence and aggression.

1.3 The document sets out the physical health monitoring that must be undertaken following the administration of parenteral medication for rapid tranquillisation.

1.4 Violence and aggression refer to a range of behaviours, actions or threats that can result in harm, hurt or injury to another person, regardless of whether the violence or aggression is physically or verbally expressed, or physical harm is sustained.

1.5 Violence and aggression are relatively common and serious occurrences in health and social care settings. Between 2013 and 2014 there were 68,683 assaults reported against NHS staff in England: 69% in mental health or learning disability settings, 27% against ambulance staff, 25% involving primary care staff and 26% involving acute hospital staff. Violence and aggression in mental health settings occur most frequently in inpatient psychiatric units (NICE NG10). Figures obtained under a Freedom of Information request from nearly two-thirds of mental health trusts in the UK indicate that assaults increased from 33,620 in 2012/13 to 42,692 in 2016/17. Assaults on mental health staff in England increased by more than a third during this time[#].

1.6 The manifestation of violence and aggression depends on a combination of intrinsic factors, such as personality characteristics and intense mental distress, and extrinsic factors, such as the attitudes and behaviours of surrounding staff and service users, the physical setting and any restrictions that limit the service user's freedom. The impact of violence and aggression is significant and diverse, adversely affecting the health and safety of the service user, other service users in the vicinity, carers and staff. Violence and aggression can also affect public opinion about services and service users and result in a strong negative impact on the overall experience of care.

1.7 The use of medication is one of several possible interventions that can be used to prevent or to manage manifestations of violence and aggression occurring in the context of mental disorders.

1.8 The National Institute for Health and Care Excellence (NICE) published its guideline, "Violence and aggression: short-term management in mental health, health and community settings [NG10]", in May 2015. This guideline included recommendations on the use of medication for the prevention and management of violence and aggression, and was an update to the previous NICE guideline CG25; "Violence: The Short-term Management of Disturbed/ Violent Behaviour in Psychiatric In-patient Settings and Emergency Departments (February 2005)".

1.9 The current document represents a synthesis of the updated NICE guideline (NG10) with the existing East London NHS Foundation Trust (ELFT) policy on rapid tranquilisation which was largely based on the previous NICE guideline (CG25).

[#] BBC News, "Assaults on mental health staff up 25% in four years", 8th October 2017.

2.0 Scope

2.1 This policy applies when using pharmacological treatment for rapid tranquillisation in adults aged 18 years and over. For guidance on the treatment of those under 18 years of age, consult the Trust's, *"Guidelines for the management of acutely disturbed children and adolescents in psychiatric settings"*.

2.2 Pharmacological interventions are one of a number of strategies used to manage violence and aggression. However, only the pharmacological management of violence and aggression falls within the scope of this policy. For information about non-pharmacological strategies, consult the relevant Trust guidance.

2.3 Medication should only be administered to a service user provided there is a clear legal basis for treatment.

2.4 This policy's requirements for physical health monitoring following parenteral administration of medication for rapid tranquillisation also apply to situations in which parenteral psychotropic medication is used but which are not considered to be rapid tranquillisation.

2.5 This policy should be used in conjunction with all other relevant Trust policies and guidelines, including;

- Consent to Treatment Policy
- Mental Capacity Act Policy
- Policy on the Use of Physical Holding Skills
- Seclusion Policy
- Guidelines for prescribing and administration of PRN psychotropic medicines
- Policy for the use of high dose antipsychotic medication
- Medicines Policy

3.0 Roles and responsibilities

Prescribers

3.1 Ensure that the choice of medication for rapid tranquillisation is clinically appropriate and legal, including taking full consideration of the service user's physical health, mental health and current legal status.

3.2 Ensure that prescriptions are clear, unambiguous and complete.

3.3 Review prescriptions for rapid tranquillisation at least once a week, and document this review in the service user's notes.

3.4 If medication for rapid tranquillisation is administered, review the prescription daily.

3.5 Ensure that service users are monitored for side effects and the therapeutic effect of medicines administered.

Nursing staff

3.6 Ensure that medication is administered correctly in accordance with the prescription.

3.7 When making decisions about the administration of medication, ensure that full consideration is given to the likely effects of the medication in light of the service user's current physical and mental health. Consideration should be given both to the intended therapeutic effects and the possible side effects of the medication.

3.8 Ensure that medication is only administered when it is legally appropriate to do so.

3.9 Monitor the service user for side effects and desired effects following the administration of medication.

Registered Nursing Associates

3.10 Are not permitted to administer rapid tranquillisation.

Are permitted to undertake the second check of intramuscular medicines alongside the registered nurse.Pharmacists

3.11 Check medicines are prescribed at the right dose and route, and are appropriate considering the service user's current physical and mental state, and other pharmacological treatments.

4.0 Terms used in this guideline

British National Formulary (BNF):

4.1 The BNF is a joint publication of the British Medical Association and the Royal Pharmaceutical Society of Great Britain, and includes key information on the selection, prescribing, dispensing and administration of medicines. It is important to use the most recent BNF information. The print edition is updated in March and in September of each year. Monthly updates are available online (https://bnf.nice.org.uk). The BNF can be accessed by clicking the BNF icon on the desktop of any Trust computer.

p.r.n. (pro re nata); 'when required':

4.2 The use of medication as part of a strategy to de-escalate or prevent situations that may lead to violence or aggression.

Rapid tranquillisation (RT):

4.3 The 2005 NICE guidance (CG25) defined rapid tranquillisation (RT) as; "The use of medication to calm/lightly sedate the service user, reduce the risk to self and/or others and achieve an optimal reduction in agitation and aggression thereby allowing a thorough psychiatric evaluation to take place and allowing comprehension and response to spoken messages throughout the intervention. Although not the overt intention, it is recognised that in attempting to calm/lightly sedate the service user, rapid tranquillisation may lead to deep sedation/anaesthesia". This definition included both oral and parenteral medication.

4.4 The updated 2015 NICE guidelines (NG10) define RT as; "The use of medication by the parenteral route if oral medication is not possible or appropriate and urgent sedation with medication is needed". This definition explicitly excludes oral medication from the NICE definition of RT.

4.5 Whilst recognising that the eventual outcome of RT may be the sedation of the service user, the Trust considers that sedation should not be viewed as the ultimate goal of the intervention. The Trust's position is that the goal of RT should be viewed from the perspective of harm-minimisation and treatment of illness. Thus, RT should be viewed as means to reduce the risk of harm from violence and aggression, rather than a means to induce unconsciousness in the service user. This reflects a more patient-centred approach than that adopted in the current 2015 NICE guideline (NG10), as well as more accurately reflecting the way RT is used in practice.

4.6 For the purpose of this policy, the Trust has adopted the following definition of RT: "The use of parenteral medication in an attempt to quickly calm the service user, in order to reduce the risk of imminent and serious violence to self or others, when appropriate psychological and behavioural approaches have not been sufficient to de-escalate acutely disturbed behaviour and the use of oral medication is not possible or appropriate".

5.0 General principles when using medication

5.1 Medication should be viewed as one of the range of interventions that can be useful in the management of violence and aggression associated with mental disorder; it should not be used on its own in the absence of other therapeutic strategies.

5.2 Medication should only be used if it is both clinically and legally appropriate to do so. This implies that a provisional or differential diagnosis will usually have been made.

5.3 All medicines have the potential to cause unwanted effects, therefore whenever medication is used, it should be used at the lowest effective dose for the shortest possible duration. BNF maximum recommended doses should only be exceeded with the permission of a consultant psychiatrist.

5.4 Medication should be part of an individualised treatment strategy formed after taking into consideration service user-specific factors.

5.5 Account must be taken of the service user's physical health, including any long-term health conditions as well as their current presentation. Wherever possible, a physical examination should

be carried out and an ECG performed before medication is administered, or as soon as possible afterwards. A note should be made of the reason if this cannot be done.

5.6 A multidisciplinary team that includes a psychiatrist, a psychiatric nurse and a specialist pharmacist should develop and document an individualised pharmacological strategy for using regular and p.r.n. medication to calm, tranquillise or sedate service users who are at risk of violence or aggression as soon as possible after admission.

5.7 The multidisciplinary team should review the pharmacological strategy and the use of medication at least once a week and more frequently if events are escalating and restrictive interventions are being planned or used. The review should include the following:

- Clarification of target symptoms
- Therapeutic response
- The likely timescale for response to medication
- The total daily dose of medication, prescribed and administered, including p.r.n. medication
- The number of and reason for any missed doses
- The emergence of unwanted effects

5.8 The review of the pharmacological strategy should be documented in the service user's notes, along with the future treatment plan.

5.9 When the risks of harm have been contained following an episode of violence, there should be a post-incident debrief to identify and address physical harm to service users or staff, ongoing risks and the emotional impact on service users and staff, including witnesses.

5.10 Encourage service users to recognise their own triggers and early warning signs of violence and aggression, and to discuss and negotiate their wishes should they become agitated. Include this information in care plans and advance statements and give a copy to the service user.

6.0 Using p.r.n. medication to prevent violence and aggression

6.1 The use of parenteral medication should be viewed as a last-line option. One of the strategies that can be employed to de-escalate or prevent situations that may lead to violence and aggression is the effective use of 'when required' (p.r.n.) medication.

6.2 The use of p.r.n. medication is governed by the Trust's, "Guidelines for prescribing and administration of PRN psychotropic medicines", which should be read in conjunction with this policy.

6.3 p.r.n. medication is normally given by the oral route. However, parenteral medication can also be used on a 'when required' basis to prevent episodes of acutely disturbed behaviour. Parenteral p.r.n. medication should only be used if the oral route has been ruled out. There should be a clear

and justifiable rationale for using parenteral medication in this way, and this rationale should be documented. If parenteral medication is administered, the same post-dose monitoring as for rapid tranquillisation should be performed, as set out in section 11.0 of this document.

6.4 Tailor p.r.n. medication to individual need and include discussion with the service user if possible.

6.5 Ensure there is clarity about the rationale and circumstances in which p.r.n. medication may be used and that these are included in the service user's care plan.

6.6 Ensure the maximum daily dose is specified and does not exceed the maximum daily dose stated in the British National Formulary (BNF) when combined with the person's regular dose or their dose for RT; unless this is authorised by a consultant psychiatrist.

6.7 Only exceed the BNF maximum daily dose (including p.r.n. dose, the standard dose and dose for rapid tranquillisation) if this is planned to achieve an agreed therapeutic goal, documented and carried out under the direction of a consultant psychiatrist. If the BNF maximum daily dose for antipsychotic medication is exceeded, the guidance in the Trust's, "Policy for the use of high dose antipsychotic medication" should be followed.

6.8 Ensure that the interval between p.r.n. doses is specified.

6.9 The multidisciplinary team should review p.r.n. medication at least once a week and, if p.r.n. medication is to be continued, the rationale for its continuation should be included in the review. If p.r.n. medication has not been used since the last review, consider stopping it.

6.10 If p.r.n. medication is given, the service user should be monitored for the desired effect and for any unwanted effects from the medication.

7.0 Using medication for rapid tranquillisation

7.1 Parenteral medication should only be used after other options for the management of violence and aggression have been exhausted. Prior to its use, a risk assessment should be conducted to establish that the risks posed by RT are outweighed by the risks of not administering medication.

7.2 Staff involved in the prescription and administration of parenteral medication should be trained in the use of cardiopulmonary resuscitation, and this training should be kept up-to-date.

7.3 The equipment required for cardiopulmonary resuscitation should be readily accessible in all clinical areas in which RT is used.

7.4 Staff involved in restraining service users should adhere to the, "Policy on the use of physical holding skills".

7.5 If parenteral medication is intended to be administered, the service user must be given the opportunity to take oral medication, if that is considered safe.

7.6 When deciding which medication to use, take into account:

- the service user's provisional or established diagnosis
- 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: BNF- recommended maximum doses should only be exceeded in extreme circumstances and with the approval of a consultant psychiatrist.
- The evidence base supporting the use of particular medicines for RT and for that diagnosis.

7.7 The 2015 NICE guideline recommends that the choice of IM medication for RT should be limited to either lorazepam on its own or haloperidol combined with promethazine. This is in contrast to the 2005 NICE guidance which stipulated that if IM medication is required, a benzodiazepine should be given along with an antipsychotic drug. Evidence from the most recent Prescribing Observatory for Mental Health- UK (POMH-UK) national audit of RT indicates that half of incidents of acute behavioural disturbance are treated with oral medication alone, and that most IM RT involves the administration of a benzodiazepine drug on its own, but that when an antipsychotic drug is used, it is more commonly the case that the antipsychotic is given with a benzodiazepine, rather than given by itself. The use of combined haloperidol and promethazine only occurred in 3% of incidents.

7.8 The current NICE guidelines (NG10; 2015) recommend the following options for use in RT;

- IM lorazepam, or;
- IM haloperidol with IM promethazine.

7.9 The Trust recognises that there will be cases where the options set out in the 2015 NICE guidelines may be deemed inappropriate or do not work. In these cases, the following options can be considered after discussion with a senior doctor:

- A combination of IM drugs from different pharmacological classes; for example, an antipsychotic plus a benzodiazepine (lorazepam)
- IM olanzapine
- IM aripiprazole
- IM midazolam
- IM promethazine used alone
- Intravenous (IV) medication (requires approval from a consultant psychiatrist)

The justification for using one of these treatment options must be documented in the service user's notes.

7.10 If there is insufficient information to guide the choice of medication for rapid tranquillisation, for example if the diagnosis of psychosis remains uncertain, or the service user has not taken antipsychotic medication before, use a benzodiazepine or promethazine in preference to an antipsychotic. If the service user has not previously received an antipsychotic, lower doses are likely to be indicated.

7.11 If there is a partial response to a particular drug, consider a further dose of the same drug.

7.12 If there is no response to particular drug, consider switching to a drug from a different pharmacological class (benzodiazepine, antipsychotic or promethazine).

7.13 Do not repeat a dose of rapid tranquillisation until the effect of the initial dose has been reviewed.

8.0 Specific drug considerations

8.1 Before prescribing, dispensing or administering parenteral medication for RT, staff must familiarise themselves with the clinical particulars for each drug set out in the most recent copy of the British National Formulary (BNF). These clinical particulars include; cautions, contraindications, side effects, method of administration, dose and interactions.

8.2 Appendix 1 contains further information about the individual drugs used in RT, including; usual doses for RT, time to peak plasma level, and elimination half-life.

8.3 Some specific considerations that must be taken into account when using particular drugs for intramuscular (IM) rapid tranquillisation (RT) are set out below.

Benzodiazepine drugs

8.4 The main risks associated with benzodiazepine drugs are the effects associated with excess dosing which can include loss of consciousness, and respiratory depression and/or arrest.

8.5 Benzodiazepines should be avoided in service users displaying evidence of significant respiratory impairment.

8.6 Benzodiazepines are usually a safer choice for RT in service users who have not previously taken an antipsychotic drug.

8.7 If there is limited information about a service user's past drug or medical history, benzodiazepine drugs are usually a safer choice than antipsychotic drugs.

8.8 Any regular benzodiazepine drugs that the service user is already taking should be taken into consideration before using a benzodiazepine for rapid tranquillisation. Be aware that the long elimination half-life of some benzodiazepines (for example, diazepam and clonazepam) may mean they only reach their peak effect after several days of repeated dosing.

8.9 Service users who have not previously been exposed to benzodiazepines may be more sensitive to the effects of the drugs.

8.10 When IM benzodiazepines are administered, flumazenil injection must be available for use on the ward.

Lorazepam (IM)

8.11 If an IM benzodiazepine is required, lorazepam should be the first-line choice.

Midazolam (IM)

8.12 IM midazolam should only be considered as an alternative to IM lorazepam if lorazepam injection is unavailable due to supply problems.

8.13 Midazolam has a fast onset of action and a short half-life (1.5-2.5 hours), and is difficult to dose in a therapeutic window avoiding over-sedation with respiratory depression. When midazolam is administered, the service user must be monitored continuously and flumazenil should be readily accessible.

Antipsychotic drugs

8.14 Before prescribing or administering antipsychotic medication for RT, it is vital that any regular antipsychotics the service user is already taking are taken into considered. The maximum BNF recommended total daily antipsychotic dose should only be exceeded on the advice of a consultant psychiatrist.

8.15 A drawback of using antipsychotic drugs is the risk of acute extrapyramidal side effects (EPSEs). This risk is higher if there has been no previous exposure to antipsychotics. If it is decided to use an antipsychotic drug for a service user with no previous exposure, a lower dose is required.

Haloperidol (IM)

8.16 The risk of developing EPSEs is higher with haloperidol than with second generation antipsychotics such as olanzapine or aripiprazole. An anticholinergic drug should always be available when IM haloperidol is used.

8.17 Promethazine is a sedating antihistamine and has an anticholinergic effect. It has been shown to reduce the incidence of EPSEs if given with haloperidol.

8.18 IM haloperidol has the potential to cause an increase in the QTc interval on the ECG, especially at high doses, thus predisposing to cardiac dysrhythmias. If there is evidence of cardiovascular disease, including a prolonged QT interval, or no electrocardiogram (ECG) has been carried out, haloperidol should be avoided. If the service user previously had an ECG, clinical judgement should be used when deciding whether this provides sufficient evidence about the service user's current cardiac status, or whether the ECG should be repeated before giving haloperidol.

Olanzapine (IM)

8.19 IM olanzapine should not be administered within one hour of a parenteral benzodiazepine drug, and a parenteral benzodiazepine drug must not be given until at least an hour has passed after the administration of IM olanzapine. This is to reduce the risk of over-sedation.

8.20 Intramuscular (IM) administration of olanzapine leads to higher plasma levels than oral administration, therefore the oral and IM doses of olanzapine are not equivalent.

8.21 When one or more factors are present that might result in slower metabolism (e.g. female gender, elderly, non-smoker) consider using a lower dose of IM olanzapine.

8.22 IM olanzapine is not available as a licensed product in the UK. The stock used in ELFT has to be imported from outside the UK. As a result, the directions on the product packaging and information leaflet may be in a language other than English. If there is lack of clarity about how the drug should be used a pharmacist should be contacted before it is administered.

Aripiprazole (IM)

8.23 The manufacturer of IM aripiprazole advises that dose adjustment is needed in the presence of medicines known to induce or inhibit hepatic enzymes. For full information about dose adjustments required due to concurrent use of interacting drugs, consult the product literature.

Promethazine (IM)

8.24 Promethazine is a sedating and anticholinergic antihistamine. It has a relatively slow onset of action (1-2 hours), but can assist sedation.

8.25 Promethazine reduces the risk of EPSEs with antipsychotics such as haloperidol, but it can prolong the QT interval and lower the seizure threshold.

8.26 Promethazine may be a useful option in a benzodiazepine-tolerant service user.

8.27 Caution should be used when promethazine is given with other sedating medication, as it can cause additional CNS-depression.

Combining drugs

8.28 Combinations of drugs should be used with caution because of the increased potential for side effects. However, a combination allows different mechanisms of action to contribute to the effect.

8.29 The combination of two different intramuscular drugs in the same pharmacological class (for example two benzodiazepine drugs, or two antipsychotic drugs) should be avoided.

8.30 It is widely recommended that haloperidol should not be given without an anticholinergic drug. NICE guidance (NG10 2015) recommends that if IM haloperidol is used, IM promethazine should be given at the same time - to reduce the risk of extrapyramidal side effects (EPSEs).

8.31 The combination of an antipsychotic with a benzodiazepine (for example, haloperidol plus lorazepam) is a widely-used option and was recommended in NICE CG15 (2005).

8.32 IM olanzapine should not be administered within one hour of a parenteral benzodiazepine drug, and a parenteral benzodiazepine drug must not be given until at least an hour has passed after the administration of IM olanzapine. This is to reduce the risk of over-sedation.

8.33 Concomitant use of two or more antipsychotics (oral or IM) should be avoided on the basis of risk associated with QTc prolongation (common to most antipsychotics). This is a particularly important consideration in RT where the service user's physical state predisposes to cardiac arrhythmia.

9.0 Intravenous medication

9.1 Intravenous (IV) medication should only be considered for RT in exceptional circumstances, when all other options have been exhausted.

9.2 If it is required, IV medication must only be given by someone trained and competent in administering drugs by this route.

9.3 The decision to administer IV medication for RT must only be taken by a consultant psychiatrist.

9.4 If IV medication is required, diazepam should normally be considered the first line choice. If IV diazepam is to be given, flumazenil must be available to administer.

9.5 For guidance on dosing, the most recent copy of the BNF and summary of product characteristics should be consulted, along with the on-call pharmacist.

9.6 Haloperidol is considered less appropriate for IV administration because of the increased risk of QTc prolongation and/or ventricular arrhythmias, in addition to sudden death, when the drug is given by this route. It is a requirement of the manufacturer's summary of product characteristics that if IV haloperidol is given, continuous ECG monitoring must be performed. Staff should consider this requirement before using IV haloperidol, bearing in mind that facilities for continuous ECG monitoring may only be available at in an acute hospital.

9.7 The service user should not be left unattended until at least an hour has passed after IV administration of RT.

10.0 Physical health monitoring following rapid tranquillisation

10.1 After rapid tranquillisation (RT), the service user's pulse, blood pressure, respiratory rate, temperature, and level of consciousness should be monitored every 15 minutes. These observations should be recorded on the Rapid Tranquillisation Monitoring Chart (Appendix 3). The 15-minute observations should also include checking the service user for other side effects from the medication and checking their hydration status.

10.2 If one or more of the service user's observations is in the amber-shaded range of the Rapid Tranquillisation Monitoring Chart, the duty doctor and the nurse in charge should be informed and the service user should be monitored continuously.

10.3 If one or more of the service user's observations is in the red-shaded range of the Rapid Tranquillisation Monitoring Chart, this should prompt an immediate, urgent referral to the local medical emergency response team (i.e. "crash team") and the emergency services.

10.4 Monitoring must be carried out at least every 15 minutes for the first 60 minutes after administration of RT, but must continue beyond this point if the service user is not ambulatory or if their physical observations are outside the acceptable range (i.e. in the 'amber' or 'red' range). Monitoring should only be stopped when there are no further concerns about the service user's physical health status.

10.5 If the service user refuses physical health observations following RT, then respiratory rate and level of consciousness should still be recorded after visually observing the service user.

10.6 The completed Rapid Tranquillisation Monitoring Form should be scanned and uploaded onto the service user's electronic record (under "Clinical documentation" on RiO), and the physical copy should be filed in the service user's notes. Local adaptations of the monitoring form, either in paper or electronic form, are acceptable provided the necessary parameters are recorded in a format that is clear and that can be uploaded to the service user's record system.

10.7 If RT is being used, a consultant psychiatrist should review all medication at least once a day.

10.8 The physical health monitoring outlined above should be carried out every time a benzodiazepine drug, antipsychotic drug or sedating antihistamine drug is administered by the intramuscular route; this is regardless of whether the administration is regarded as rapid tranquillisation or not.

11.0 Rapid tranquillisation during seclusion

11.1 If rapid tranquillisation (RT) is needed while a service user is secluded, undertake with caution following the recommendations above and:

- be aware of and prepared to address any complications associated with RT
- ensure the service user is observed within eyesight by a trained staff member
- undertake a risk assessment and consider ending the seclusion when RT has taken effect.

12.0 Rapid tranquillisation for older people

12.1 Older adults may be more sensitive to the pharmacological effects, both the desired effects and side effects, of the medication used for rapid tranquillisation. This may require the use of lower

doses of medication in older adults. The dosing guidance in the BNF and in the product literature should always be followed.

12.2 Those least tolerant are older people who are clearly chronically frail or with concurrent medical illness including dementia and especially Lewy body dementia. Therefore, frail elderly should be given only the lowest dose of the tranquilliser dose range.

12.3 Lorazepam should be considered first line for acute behavioural disturbances.

12.4 Antipsychotics can be considered for service users who have a confirmed history of previous antipsychotic exposure. However, their use requires particular caution in those with cardiac or circulatory disease and they should be avoided in service users with dementia, particularly those with Lewy body dementia. First generation antipsychotics (for example, haloperidol) should be avoided due to the high incidence of extrapyramidal side effects.

12.5 For service users with no confirmed history of antipsychotic-use, or who have a diagnosis of dementia, antipsychotics should only be used when other pharmacological treatments have either been unsuccessful or are inappropriate.

13.0 Rapid tranquillisation for pregnant women

13.1 In addition to the guidance outlined above, the following principles apply when using rapid tranquillisation (RT) for women who are pregnant.

13.2 A pregnant woman should never be secluded after administration of RT.

13.3 Restraint procedures should be adapted to avoid possible harm to the unborn child and the mother. The ELFT perinatal team should be contacted for advice and training.

13.4 Any unit onto which a pregnant woman is admitted should have access to beanbags for use during RT. If RT is being given, the pregnant woman should be lowered onto the beanbag so that she is supported and not allowed to lie on her back as this can lead to physical problems resulting from obstruction of major blood vessels.

13.5 When a female service user is known to be pregnant, a care plan outlining the medication to be used should be written.

13.6 Decisions around choice of medication should be made on an individual service user basis taking into account both the risks to the mother and to the unborn child.

13.7 Intramuscular injections for RT may be administered into the gluteal muscle or lateral thigh.

13.8 After RT the service user must be reviewed by a midwife to ensure that the foetus has not been harmed by the procedure.

13.9 Rapid deterioration in mental state towards the end of pregnancy may indicate that the mother is going into labour.

13.10 During labour if the woman becomes acutely disturbed; her care should be managed in close collaboration with a paediatrician, an anaesthetist and psychiatry.

13.11 All interventions should be documented and communicated verbally in handover to all professionals involved including psychiatry, midwife and paediatrics.

14.0 Zuclopenthixol acetate (*Clopixol Acuphase®*)

14.1 Zuclopenthixol acetate (*Clopixol Acuphase®*) is not considered an appropriate first-line drug for use for RT. Onset of action does not occur until two hours after injection, and only peaks after 12 hours.

14.2 Zuclopenthixol acetate may occasionally be used as part of a medium-term strategy if a service user responds to other IM antipsychotic medication and it is anticipated that they will require further repeated IM injections.

14.3 The decision to use zuclopenthixol acetate should only be taken by a consultant psychiatrist.

14.4 Zuclopenthixol acetate should **never** be used in service users who are:

- Neuroleptic-naïve (that is, who have not taken an antipsychotic drug before)
- Sensitive to extrapyramidal side effects
- Unconscious
- Pregnant
- Suffering from hepatic or renal impairment, or cardiac disease.

14.5 Zuclopenthixol acetate should never be administered:

- In an attempt to hasten the antipsychotic effect of other antipsychotic therapy
- At the same time as other short-acting parenteral antipsychotics or benzodiazepines (may lead to over-sedation which is difficult to reverse)

14.6 As with all oil-based injections it is important to ensure, by aspiration before injection, that inadvertent intravascular entry does not occur.

14.7 With zuclopenthixol acetate, sedative effects usually begin after 2 hours, peak after 12 hours and last for up to 72 hours.

14.8 For dosing and administration guidance, see the most recent copy of the BNF and the summary of product characteristics.

Monitoring

14.9 Ensure that the physical and mental health of the service user is assessed before each administration of zuclopenthixol acetate.

14.10 The service user's physical health observations should be monitored at 15 minutes post-injection, then again at 30 minutes post-injection and then at least every 3 hours for at least 48 hours. Monitoring should continue beyond 48 hours if there are any further concerns about the service user's physical health.

14.11 These observations should be recorded on the Clopixol Acuphase® monitoring chart (see Appendix 5).

14.12 If patient has declined, is asleep or is unsafe to approach (including seclusion), then respiratory rate and level of consciousness MUST be recorded as a minimum.

14.13 Once completed, the Clopixol Acuphase® monitoring chart should be uploaded onto Rio.

14.14 It is particularly important to monitor the service user's fluid intake after they have been given zuclopenthixol acetate. If the service user is sedated for a long time, fluid intake may decrease; increasing the risk of dehydration.

15.0 Flumazenil for reversal of benzodiazepine-induced respiratory depression

15.1 Flumazenil is a benzodiazepine antagonist which can be used to reverse the sedative and respiratory-depressing effect of benzodiazepine drugs.

15.2 Wards on which intramuscular (IM) benzodiazepines are used for rapid tranquillisation (RT) must be able to access flumazenil quickly in the event of it being needed. Flumazenil is kept in the "non-cardiac arrest" packs of emergency medication on all ELFT responder wards.

15.3 The table in Appendix 2 sets out the indication, contraindications, cautions and treatment pathway for the use of flumazenil.

15.4 Rapid reversal of the effects of benzodiazepines can be dangerous. For example, if a service user is taking benzodiazepines to control seizures, or has been taking a benzodiazepine for a long time, rapid reversal of the drug's activity has the potential to induce seizures. It is therefore important that before flumazenil is administered, the risks of giving the drug have been decided to be less that the risks of not giving it.

15.5 Flumazenil must be given by the intravenous route, and so should only be administered by people who have been trained and are competent to administer medication by this route.

15.6 Flumazenil is short-acting, meaning that its effects may wear-off before the effects of the causative benzodiazepine have worn off. This may mean that repeated doses of flumazenil will be necessary.

Service users who are given flumazenil should continue to be monitored even after their respiratory rate has returned to normal.

15.7 Flumazenil will not reverse respiratory depression that is caused by anything other than a benzodiazepine drug. For example, it has no effect on opioid-induced respiratory depression.

15.8 Flumazenil should not be used in the presence of a mixed overdose of benzodiazepines and tricyclic or tetracyclic antidepressants. In these cases, the benzodiazepine may be exerting a protective effect, lowering the risk of convulsions caused by the tricyclic/tetracyclic overdose.

16.0 References

Abilify (aripiprazole) 7.5 mg/ml solution for injection (intramuscular), Summary of Product Characteristics, Otsuka, last updated 21st November 2016, available from: https://www.medicines.org.uk/ (last accessed 24th August 2017).

AHFS (American Hospital Formulary Service) Drug Information® monographs. Publisher: American Society of Health System Pharmacists, Inc. Ed: McEvoy GK. Online resource available to subscribers via: www.medicinescomplete.com (last accessed 24th August 2017).

Ativan® (lorazepam) injection, Summary of Product Characteristics, Pfizer Ltd, last updated 10th June 2014, available from: https://www.medicines.org.uk/ (last accessed 23/8/17).

British Medical Association and Royal Pharmaceutical Society of Great Britain; "British National Formulary" online edition, Pharmaceutical Press, last updated 2nd August 2017. Available from: https://bnf.nice.org.uk/ (accessed 23rd August 2017).

Haloperidol Injection BP 5mg/ml, Summary of Product Characteristics, Concordia International, last updated 16th January 2017, available from: https://www.medicines.org.uk/ (last accessed 15th May 2020).

Hypnovel (midazolam) 10mg/2ml solution for injection, Summary of Product Characteristics, Roche, last updated 11th February 2015, available from: https://www.medicines.org.uk/ (last accessed 24th August 2017).

NICE 2005; "Clinical Practice Guidelines for Violence: The Short-term Management of Disturbed/ Violent Behaviour in Psychiatric In-patient Settings and Emergency Departments", National Institute for Health and Care Excellence (NICE), February 2005.

NICE guideline 10 (NICE NG10); "Violence and aggression: short-term management in mental health, health and community settings", National Institute for Health and Care Excellence (NICE), May 2015.

Phenergan (promethazine) Injection, Summary of Product Characteristics, Sanofi, last updated 26th September 2016, available from: https://www.medicines.org.uk/ (last accessed 24th August 2017).

Prescribing Observatory for Mental Health- UK (POMH-UK); "Topic 16a: Rapid tranquillisation in the context of the pharmacological management of acutely disturbed behaviour" (CCQI263), Royal College of Psychiatrists, June 2017.

Royal Pharmaceutical Society, Martindale: The Complete Drug Reference- drug monographs. Publisher: Pharmaceutical Press. Ed: Brayfield A. Online resource available to subscribers via www.medicinescomplete.com. (last accessed 24th August 2017).

Taylor D, Paton C, and Kapur S; "*The Maudsley Prescribing Guidelines in Psychiatry*", 12th edition, Wiley Blackwell, April 2015.

Appendix 1

Information about medication for rapid tranquillisation

Table 1: NICE-recommended intramuscular (IM) treatment options for rapid tranquillisation (RT)

The table below sets out the medications for RT that are specifically recommended in NICE guideline 10 (NICE NG10); "Violence and aggression: short-term management in mental health, health and community settings". Consult the most recent version of the BNF for full information about each of the drugs.

	Lorazepam (IM)	Haloperidol (IM)	Promethazine (IM)*
Type of drug	Benzodiazepine	First generation antipsychotic	Sedating antihistamine
Adult dose	25-30 micrograms/kg every 6 hours (usual dose 1.5–2.5 mg every 6 hours)	5-10mg (max. 20mg/day)	25-50mg (max. 100mg/day)
Elderly dose	12.5-15 micrograms/kg every 6 hours (usual dose 0.75–1.25 mg every 6 hours)	2.5mg-5mg (max. 5mg/day)	25-50mg (max. 100mg/day)
Time to peak plasma level	60-90 minutes	10-20 minutes	2-3 hours
Elimination half-life	12-16 hours	20 hours	5-14 hours
Notes	Usually a safer choice in people whose medical history is unknown, and in those who have not previously taken an antipsychotic drug. Ativan® preparation: mix 1:1 with water for injection before injecting. Ensure flumazenil injection to hand in case of respiratory depression.	Avoid in people who have not taken an antipsychotic before (increased risk of acute dystonia). Ensure IM procyclidine to hand for treatment of acute dystonia. Risk of acute dystonia is reduced if IM promethazine is given at the same time as IM haloperidol. If there is evidence of cardiovascular disease, including a prolonged QTc interval, or no electrocardiogram (ECG) has been carried out, haloperidol should be avoided. Take into account any regular antipsychotic medication that the service user is taking. Do not exceed BNF max. daily antipsychotic dose and avoid combining antipsychotics.	Promethazine requires *deep* IM injection. Reduces the risk of acute dystonia if given with IM haloperidol.

*NICE NG10 (2015) only recommends promethazine as an additional treatment to be given at the same time as haloperidol to reduce the risk of extrapyramidal side effects. NICE does not specifically recommend the use of promethazine on its own.

Table 2: Other intramuscular (IM) treatment options for rapid tranquillisation (RT)

The following intramuscular medications should only be considered for use in rapid tranquillisation if the NICE-recommended treatment options are clinically inappropriate, unavailable or have been ineffective. Consult the most recent version of the BNF for full information about each of the drugs.

	Midazolam (IM)	Olanzapine (IM)	Aripiprazole (IM)
Type of drug	Benzodiazepine	Second generation antipsychotic	Second generation antipsychotic
Adult dose	70-100 microgram/kg* (max. 15mg/day)	5-10mg (max. 20mg/day for 3 days)	5.25-9.75mg (max. 30mg/day)
Elderly dose	25-50 micrograms/kg* (max. 11.25mg/day)	2.5-5mg (max. 20mg/day for 3 days)	Not specified: consider using lower dose
Time to peak plasma level	30 minutes	15-45 minutes	1-3 hours
Elimination half-life	1.5-2.5 hours (longer in elderly)	30-38 hours	3-6 days
Notes	**Caution:** Midazolam can quickly lead to a deep sedation with risk of respiratory depression. Before administration, ensure that flumazenil injection is available. Midazolam should only be considered as an alternative to IM lorazepam if lorazepam is unavailable due to supply issues. *Note: Midazolam is not licensed for the control of agitation or aggression. The main literature evidence for the use of midazolam in RT comes from the TREC study[#] in which single doses of 7.5-15mg of midazolam were used. However, anecdotal evidence from the use of midazolam in ELFT has found that lower doses than this are generally effective. The dose ranges stated above are based on those normally used for surgical premedication. There may be wide inter-patient variability in the level of sedation achieved; close and continuous monitoring of the service user after administration of midazolam is essential.	**Caution:** leave at least one hour between administration of olanzapine intramuscular injection and administration of a parenteral benzodiazepine When one or more factors are present that might result in slower metabolism (e.g. female gender, elderly, non-smoker) consider using lower dose. IM administration leads to higher plasma levels of olanzapine than oral administration, therefore oral and IM doses are not equivalent.	Manufacturer advises to double the dose with concurrent use of potent inducers of CYP3A4 , and to reduce dose by half with concurrent use of potent inhibitors of CYP3A4 or CYP2D6. For dose adjustments due to concurrent use of interacting drugs—consult product literature.

[#]Rapid tranquillisation for agitated patients in emergency psychiatric rooms: a randomised trial of midazolam versus haloperidol plus promethazine BMJ 2003; 327:708. doi: https://doi.org/10.1136/bmj.327.7417.708

Appendix 2

Guidance on the use of flumazenil

Guidance on the use of flumazenil to treat benzodiazepine-induced respiratory depression

Indication	Respiratory rate less than 10 breaths per minute following administration of a benzodiazepine
Contraindications	• Service users receiving benzodiazepines for the treatment of a potentially life-threatening condition (e.g. increased of intracranial pressure, or epilepsy). • In mixed intoxications with benzodiazepines and tricyclic and/or tetracyclic antidepressants, the toxicity of the antidepressants can be masked by protective benzodiazepine effects. In the presence of symptoms of severe intoxication with tricyclics/tetracyclics, flumazenil should not be used to reverse benzodiazepine effect.
Cautions	• Doses should be carefully titrated in hepatic impairment. • The antagonistic effect of flumazenil is specific to benzodiazepines; it will have no effect if the respiratory depression is caused by other substances. • As the action of flumazenil is usually shorter than that of benzodiazepines, and sedation may possibly recur, the service user should remain closely monitored until the effect of flumazenil has worn off. • In service users treated for long periods with high doses of benzodiazepines, the advantages of the use of flumazenil should be weighed against the risk of withdrawal symptoms, which may include seizures.
Treatment pathway	If the service user has a respiratory rate of less than 10 breaths per minutes following the administration of a benzodiazepine, and it has been decided that administering flumazenil will pose less risk than not administering flumazenil: 1) Contact 999 and request ambulance, and contact the Rapid Response Team and duty doctor and ask to attend ward immediately 2) Initially administer 200 micrograms flumazenil ***intravenously*** over 15 seconds 3) If required level of consciousness not achieved after 60 seconds, then give a subsequent dose of 100 micrograms over 10 seconds. 4) Repeated doses of 100 microgram can be given every 60 seconds if necessary 5) The maximum dose of flumazenil is 1 milligram in 24 hours (i.e. one initial dose followed by eight subsequent doses) 6) Continue to monitor respiratory rate until it returns to baseline level. 7) Flumazenil has a short half-life and respiratory function may recover then deteriorate again. 8) If respiratory rate does not return to normal or service user is not alert after initial doses given, assume that sedation is due to some other cause.

References:

- The Maudsley Prescribing Guidelines in Psychiatry, 12th Edition, Taylor *et al*, 2015; "*Guidelines for the use of flumazenil"*.
- Flumazenil 0.1mg/ml solution for injection, Summary of Product Characteristics, Consilient Health Ltd. Last updated: 6th July 2017. Available from: www.medicines.org.uk

Appendix 3

Rapid tranquillisation monitoring chart

Rapid Tranquillisation Monitoring Chart

Service user name:	Ward:	RiO number:	DOB:
Today's date:	Time monitoring initiated:	Time monitoring stopped:	

Instructions:

- If the service user consents to physical examination, **ALL** observations on this chart should be recorded. If observations are refused, then **respiratory rate** and level of **consciousness** should still be recorded.
- Observations in the **AMBER** range: refer to ward manager and a doctor; start continuous monitoring
- Observations in **RED** range: call ambulance and crash team

		Base line	15 mins	30 mins	45 mins	60 mins	If service user ambulatory and stable, doctor and nurse in-charge to review to consider discontinuing observations. Otherwise monitoring should continue until service user is ambulatory and stable	75 mins	90 mins	105 mins	120 mins	135 mins	150 mins	165 mins	180 mins
Temperature	>38°C														
	37.5-38°C														
	36-37.4°C														
	35-35.9°C														
	<35°C														
Respiratory rate	>25														
	20-25														
	5-19														
	<5														
Blood pressure ↔	>190														
	180														
	170														
	160														
	150														
	140														
	130														
	120														
	110														
	100														
	90														
	80														
	70														
	60														
	<50														
Heart rate	>190														
	160-189														
	50-159														
	<50														
O_2	90-100%														
	<90%														
Hydration	Well hydrated														
	Poorly hydrated														
Side effects	No side effects														
	Signs of side effects														
Consciousness	Asleep + unrousable														
	Asleep but rousable														
	Awake + calm														
	Awake + active														

Appendix 4

Source list for pharmacokinetic and drug dosing information

Table 1: Guide to abbreviations/references sources used to obtain the information set out in table 2

Abbreviation /reference source	Description
AHFS	"AHFS (American Hospital Formulary Service) Drug Information® monographs": drug information published by the American Society of Health System Pharmacists. Available online to subscribers via: www.medicinescomplete.com
BNF	"British National Formulary": joint publication of the British Medical Association and the Royal Pharmaceutical Society, and includes key information on the selection, prescribing, dispensing and administration of medicines. It is important to use the most recent BNF information for making clinical decisions. The print edition of the BNF is updated in March and September each year. Monthly updates are provided online (https://bnf.nice.org.uk).
Martindale	"Martindale: The Complete Drug Reference": drug information resource published through the Royal Pharmaceutical Society's Pharmaceutical Press. Available online to subscribers via: www.medicinescomplete.com
SPC	"Summary of product characteristics": the detailed healthcare professional information sheet produced by the drug manufacturer for products that are licensed in the UK. Freely accessible via: www.medicines.org.uk

Table 2: List of the sources that were used to obtain the drug dosing and pharmacokinetic information on which the guidance in the "Rapid Tranquillisation of Adults and Older People Policy" was based. Drugs are listed in the order in which they appear in the main body policy document.

Drug	Source	Last accessed	Link used to access	Source last updated	Information
Lorazepam	BNF monograph	23/8/17	https://bnf.nice.org.uk/drug/lorazepam.html	2/8/17	Indication: "acute panic attacks" "Adult dose: By intramuscular injection, or by slow intravenous injection; 25–30 micrograms/kg every 6 hours if required; usual dose 1.5–2.5 mg every 6 hours if required, intravenous injection to be administered into a large vein, only use intramuscular route when oral and intravenous routes not possible". Elderly dose: no separate elderly dose stated.
Lorazepam	SPC: Ativan® injection	23/8/17	https://www.medicines.org.uk/emc/medicine/2196	10/6/14	Indication: acute anxiety Dose: "Adults: 0.025-0.03mg/kg (1.75-2.1mg for an average 70kg man). Repeat 6 hourly." No separate elderly dose stated. Further info: recommends 1:1 dilution with water for injection before IM administration. Pharmacokinetic information: "Ativan Injection is readily absorbed when given intramuscularly. Peak plasma concentrations occur approximately 60-90 minutes following intramuscular administration. Ativan is metabolised by a simple one-step process to a pharmacologically inactive glucuronide. There is minimal risk of accumulation after repeated doses, giving a wide margin of safety. There are no major active metabolites. The elimination half-life is about 12-16 hours when given intramuscularly or intravenously".
Lorazepam	Martindale monograph	23/8/17	https://www.medicinescomplete.com/mc/martindale/current/7060-y.htm	11/10/13	"Lorazepam is readily absorbed from the gastrointestinal tract after oral doses, with a bioavailability of about 90%; peak plasma concentrations occur about 2 hours after an oral dose. The absorption profile after intramuscular injection is similar to that after oral dosage. Lorazepam is about 85% bound to plasma proteins. It crosses the blood-brain barrier and the placenta; it is also distributed into breast milk. Lorazepam is metabolised in the liver to the inactive glucuronide, and excreted in the urine. The elimination half-life has been reported to range from about 10 to 20 hours."
Haloperidol	BNF monograph	24/8/17	https://bnf.nice.org.uk/drug/haloperidol.html	2/8/17	Indication: "Rapid control of severe acute psychomotor agitation associated with psychotic disorder or manic episodes of bipolar 1 disorder (when oral therapy is not appropriate)" Route: "By intramuscular injection" "For Adult: 5mg, dose may be repeated hourly if required- up to 15mg daily is usually sufficient; continued use should be evaluated early in treatment; maximum 20mg per day". "For Elderly: 2.5mg, dose may be repeated hourly if required up to maximum 5mg daily, doses above 5mg daily should only be considered in patients who have tolerated higher doses and after reassessment of the individual benefit- risk; continues use should be evaluated early in treatment".

Haloperidol	SPC: Haloperidol Injection BP 5mg/ml	24/8/17	https://www.medicines.org.uk/emc/medicine/23005	16/1/17	"Absorption: Haloperidol is well absorbed from the intramuscular sites. Distribution: Variable bioavailability is likely due to the extent of first-pass hepatic metabolism. Metabolism is by oxidative dealkylation. Haloperidol is extensively bound to plasma proteins, is widely distributed throughout the body and crosses the blood-brain barrier. Elimination: Metabolites of haloperidol appear to be inactive and excretion occurs via urine and faeces. The elimination half-life is approximately 20hours."
Haloperidol	Martindale monograph	24/8/17	https://www.medicinescomplete.com/mc/martindale/current/ms-18332-f.htm	11/11/13	"It is metabolised in the liver and is excreted in the urine and, via the bile, in the faeces; there is evidence of enterohepatic recycling. Owing to first-pass metabolism in the liver, plasma concentrations after oral doses are lower than those after intramuscular injection. Moreover, there is wide intersubject variation in plasma concentrations of haloperidol. In practice, however, no strong correlation has been found between plasma concentrations of haloperidol and its therapeutic effect. Routes of metabolism of haloperidol include oxidative N-dealkylation, particularly via the cytochrome P450 isoenzymes CYP3A4 and CYP2D6, glucuronidation, and reduction of the ketone group to form an alcohol known as reduced haloperidol. Metabolites are ultimately conjugated with glycine. Haloperidol has been reported to have a plasma elimination half-life ranging from about 12 to 38 hours after oral doses. Haloperidol is about 92% bound to plasma proteins. It is widely distributed in the body and crosses the blood-brain barrier. Haloperidol is distributed into breast milk."
Haloperidol	AHFS monograph	24/8/17	https://www.medicinescomplete.com/mc/ahfs/2010/a382180.htm	8/8/17	Absorption: "Following IM administration of haloperidol lactate, peak plasma haloperidol concentrations occur within 10–20 minutes and peak pharmacologic action occurs within 30–45 minutes; in acutely agitated patients, control of psychotic manifestations may become apparent within 30–60 minutes, with substantial improvement often occurring within 2–3 hours. Haloperidol concentrations are detectable in plasma for several weeks following administration of a single dose of the drug".
Promethazine	BNF monograph	24/8/17	https://bnf.nice.org.uk/drug/promethazine-hydrochloride.html	2/8/17	Indication: "Sedation (short-term use)" Route: "By deep intramuscular injection" Dose: "For Adult: 25–50 mg." Elderly dose: no separate elderly dose stated.
Promethazine	SPC: Phenergan ® injection	24/8/17	https://www.medicines.org.uk/emc/medicine/1669	26/9/16	"Route of administration: Intramuscular or intravenous (after dilution) The usual dose is 25 - 50 mg by deep intramuscular injection, or, in emergency, by slow intravenous injection after dilution of the 2.5% solution to 10 times its volume with water for injections immediately before use. Maximum parenteral dose 100 mg. Elderly: No specific dosage recommendations". "Pharmacokinetic properties: Promethazine is slowly excreted via urine and bile. It is distributed widely in the body. It enters the brain and crosses the placenta. Phenothiazines pass into the milk at low concentrations."
Promethazine	Martindale monograph	24/8/17	https://www.medicinescomplete.com/mc/martindale/current/ms-6101-r.htm#m6101-r	5/12/13	"The usual parenteral dose for all indications apart from nausea and vomiting is 25 to 50 mg; a dose of 100 mg should not be exceeded." "Promethazine is well absorbed after oral or intramuscular doses and peak plasma concentrations occur 2 to 3 hours after a dose by these routes, although there is low systemic bioavailability after oral doses, due to high first-pass metabolism in the liver. Promethazine crosses the blood-brain barrier and the placenta, and is distributed into breast milk. Values ranging from 76 to 93% have been reported for plasma-protein binding. Promethazine undergoes extensive metabolism, mainly to promethazine sulfoxide, and also to N-desmethylpromethazine. It is excreted slowly via the urine and bile, chiefly as metabolites. Elimination half-lives of 5 to 14 hours have been reported."
Midazolam	BNF monograph	24/8/17	https://bnf.nice.org.uk/drug/midazolam.html	2/8/17	Unlicensed for treatment and aggression. Only intramuscular dosing information is for the indication of "premedication" i.e. for preparation of a patient for surgery. "Indication: premedication. By deep intramuscular injection: For Adult: 70–100 micrograms/kg, to be administered 20–60 minutes before induction, for debilitated patients, use elderly dose. For Elderly: 25–50 micrograms/kg, to be administered 20–60 minutes before induction."
Midazolam	SPC: Hypnovel 10mg/2ml solution for injection	24/8/17	https://www.medicines.org.uk/emc/medicine/1692	11/2/15	Unlicensed for treatment and aggression. Only intramuscular dosing information is for the indication of "premedication" i.e. for preparation of a patient for surgery. "Premedication with midazolam given shortly before a procedure produces sedation (induction of sleepiness or drowsiness and relief of apprehension) and preoperative impairment of memory. Midazolam can also be administered in combination with anticholinergics. For this indication midazolam should be administered i.v. or i.m., deep into a large muscle mass 20 to 60 minutes before induction of anaesthesia, or preferably via the rectal route in children (see below). Close and continuous monitoring of the patients after administration of premedication is mandatory as interindividual sensitivity varies and symptoms of overdose may occur."

					"Adults: For preoperative sedation and to impair memory of preoperative events, the recommended dose for adults of ASA Physical Status I & II and below 60 years is 1-2 mg i.v. repeated as needed, or 0.07 to 0.1 mg/kg administered i.m. The dose must be reduced and individualised when midazolam is administered to adults over 60 years of age, debilitated or chronically ill patients. The recommended initial i.v. dose is 0.5 mg and should be slowly uptitrated as needed. A dose of 0.025 to 0.05 mg/kg administered i.m. is recommended. In case of concomitant administration of narcotics the midazolam dose should be reduced. The usual dose is 2 to 3 mg." "Absorption after i.m. injection: Absorption of midazolam from the muscle tissue is rapid and complete. Maximum plasma concentrations are reached within 30 minutes. The absolute bioavailability after i.m. injection is over 90%." "Elimination: In healthy volunteers, the elimination half-life of midazolam is between 1.5 - 2.5 hours. Plasma clearance is in the range of 300 - 500ml/min. Midazolam is excreted mainly by renal route (60 - 80% of the injected dose) and recovered as glucuroconjugated alpha-hydroxymidazolam. Less than 1% of the dose is recovered in urine as unchanged drug. The elimination half-life of alpha-hydroxy-midazolam is shorter than 1 hour. When midazolam is given by i.v. infusion, its elimination kinetics do not differ from those following bolus injection. Elderly: In adults over 60 years of age, the elimination half-life may be prolonged up to four times."
Midazolam	Martindale monograph	24/8/17	https://www.medicinescomplete.com/mc/martindale/current/ms-13499-v.htm#m13499-v	n/a	"Absorption of midazolam is rapid, peak plasma concentrations occurring within 20 to 60 minutes of a dose, depending on the route". "Midazolam usually has a short elimination half-life of about 1.5 to 2.5 hours"
Midazolam	AHFS monograph	24/8/17	https://www.medicinescomplete.com/mc/ahfs/current/a387008.htm		No information on using midazolam for violence and aggression. "For preoperative sedation, anxiolysis and anterograde amnesia in good-risk (e.g., ASA Physical Status I and II) adults younger than 60 years of age, the usual IM dose of midazolam is 70–80 mcg/kg (about 5 mg) administered approximately 30–60 minutes prior to surgery. The dosage must be individualized and reduced when IM midazolam is administered to patients with chronic obstructive pulmonary disease, other higher-risk surgical patients, patients 60 years of age or older, and patients who have received opiate agonists or other CNS depressants concomitantly. In a study in patients 60 years of age or older who did not receive concomitant opiate agonist therapy, IM doses of 2–3 mg (20–50 mcg/kg) reportedly produced adequate sedation during the preoperative period; the manufacturer states that an IM midazolam dose of 1 mg may be sufficient in some geriatric patients if the anticipated intensity and duration of sedation is less critical.
Olanzapine	BNF monograph	24/8/17	https://bnf.nice.org.uk/drug/olanzapine.html	2/8/17	Indication: "Control of agitation and disturbed behaviour in schizophrenia or mania". "By intramuscular injection: For Adult: Initially 5–10 mg for 1 dose; usual dose 10 mg for 1 dose, followed by 5–10 mg after 2 hours if required, maximum 3 injections daily for 3 days; maximum daily combined oral and parenteral dose 20 mg, when one or more factors present that might result in slower metabolism (e.g. female gender, elderly, non-smoker) consider lower initial dose and more gradual dose increase. For Elderly: Initially 2.5–5 mg, followed by 2.5–5 mg after 2 hours if required, maximum 3 injections daily for 3 days; maximum daily combined oral and parenteral dose 20 mg, when one or more factors present that might result in slower metabolism (e.g. female gender, elderly, non-smoker) consider lower initial dose and more gradual dose increase".
Olanzapine	SPC	N/A	N/A	N/A	No licensed product available in UK, therefore no summary of product characteristics available.
Olanzapine	Martindale monograph	24/8/17	https://www.medicinescomplete.com/mc/martindale/current/ms-16785-l.htm#m16785-l	18/8/10	"For the rapid control of agitation and disturbed behaviour in patients with schizophrenia or mania, olanzapine may be given intramuscularly in an initial dose of 5 to 10 mg followed by 5 to 10 mg as required after 2 hours. Not more than 3 injections should be given in any 24-hour period and the maximum daily dose, including olanzapine given orally, should not exceed 20 mg. Injections may be given for a maximum of 3 days but transfer to oral therapy should be started as soon as possible. The metabolism of olanzapine might be slower in female, elderly, or non-smoking patients; if more than one of these factors is present, a lower initial dose (e.g. 5 mg daily if given orally) and a more gradual dose escalation should be considered. The intramuscular dose should be reduced by half in the elderly." "Peak plasma concentrations occur about 5 to 8 hours after oral doses and about 15 to 45 minutes after an intramuscular dose. Olanzapine is about 93% bound to plasma proteins. It is extensively metabolised in the liver, mainly by direct glucuronidation and by oxidation mediated through the cytochrome P450 isoenzymes CYP1A2, and, to a lesser extent, CYP2D6. The 2 major metabolites, 10-N-glucuronide and 4'-N-desmethyl olanzapine, appear to be inactive. About 57% of a dose is excreted in the urine, mainly as metabolites, and about 30% appears in the faeces. The mean plasma elimination half-life has been variously reported to be about 30 to 38 hours; half-lives tend to be longer in female than in male patients. Olanzapine is distributed into

					breast milk."
Aripiprazole	BNF monograph	24/8/17	https://bnf.nice.org.uk/drug/aripiprazole.html	2/8/17	Indication: "Control of agitation and disturbed behaviour in schizophrenia" "By intramuscular injection: For Adult: Initially 5.25–15 mg for 1 dose, alternatively usual dose 9.75 mg for 1 dose, followed by 5.25–15 mg after 2 hours if required, maximum 3 injections daily; maximum daily combined oral and parenteral dose 30 mg." Elderly dose: no separate elderly dose stated. "With intramuscular use: For dose adjustments due to concurrent use of interacting drugs—consult product literature".
Aripiprazole	SPC: Abilify 7.5 mg/ml solution for injection (intramuscular)	24/8/17	http://www.medicines.org.uk/emc/medicine/20802	21/11/16	"Adults: The recommended initial dose for ABILIFY solution for injection is 9.75 mg (1.3 ml), administered as a single intramuscular injection. The effective dose range of ABILIFY solution for injection is 5.25-15 mg as a single injection. A lower dose of 5.25 mg (0.7 ml) may be given, on the basis of individual clinical status, which should also include consideration of medicinal products already administered either for maintenance or acute treatment (see section 4.5). A second injection may be administered 2 hours after the first injection, on the basis of individual clinical status and no more than three injections should be given in any 24-hour period. The maximum daily dose of aripiprazole is 30 mg (including all formulations of ABILIFY)." "Elderly: The effectiveness of ABILIFY solution for injection in patients aged 65 years and older has not been established. Owing to the greater sensitivity of this population, a lower starting dose should be considered when clinical factors warrant." "Absorption: ABILIFY solution for injection administered intramuscularly as a single-dose to healthy subjects is well absorbed and has an absolute bioavailability of 100 %. The aripiprazole AUC in the first 2 hours after an intramuscular injection was 90 % greater than the AUC after the same dose as a tablet; systemic exposure was generally similar between the 2 formulations. In 2 studies in healthy subjects the median times to the peak plasma concentrations were 1 and 3 hours after dosing." "Elimination: The mean elimination half-lives for aripiprazole are approximately 75 hours in extensive metabolisers of CYP2D6 and approximately 146 hours in poor metabolisers of CYP2D6."
Aripiprazole	Martindale monograph	24/8/17	https://www.medicinescomplete.com/mc/martindale/current/ms-5433-w.htm	11/1/17	"After intramuscular injection, peak plasma concentrations occur between 1 to 3 hours. Bioavailability is reported to be 87% with oral tablets and 100% with the intramuscular injection; it is widely distributed. Aripiprazole is metabolised mainly in the liver and pathways involved include dehydrogenation and hydroxylation, via the cytochrome P450 isoenzymes CYP3A4 and CYP2D6, and N-dealkylation, via CYP3A4. The major metabolite, dehydro-aripiprazole, is also active and represents about 40% of the plasma levels of aripiprazole. The mean elimination half-lives of aripiprazole and dehydro-aripiprazole are about 75 and 95 hours, respectively; in a minority of poor metabolisers the half-life of aripiprazole may be extended to about 146 hours. Protein binding of aripiprazole and its major metabolite is about 99%, mainly to albumin. Elimination is mostly in the faeces (about 55%), with about 25% of a dose appearing in the urine, mainly in the form of metabolites".

Appendix 5

Zuclopenthixol acetate (Clopixol Acuphase®) monitoring form

Clopixol Acuphase injection (Zuclopenthixol Acetate) Monitoring chart

Service user name:	Ward:	RiO number:	DOB:
Today's date:	**Dose of drug administered:**	**Time monitoring initiated (baseline):**	**Time monitoring stopped:**

Instructions:

- If the service user consents to physical examination, **ALL** observations on this chart should be recorded by ticking the appropriate boxes. Document on Rio for hydration and side effects if **AMBER.**
- Observations in the **AMBER** range: refer to ward manager and a doctor; start continuous monitoring.
- Observations in **RED** range: call ambulance and crash team.
- If patient has **declined**, is **asleep** or is **unsafe** to approach (including **seclusion**), then respiratory rate and level of consciousness **MUST** be recorded as a minimum (use key shown →).
- If patient is administered a subsequent Acuphase dose within 48 hours, please start a new monitoring chart.
- Monitoring should continue beyond 48 hours if there are any further concerns about the service users physical health.

KEY
Insert number if patient:

1= Declined
2 = Asleep
3 = Unsafe

Time intervals		Base line	FROM BASELINE																
			15 mins	30 mins	3hrs	6hrs	9hrs	12hrs	15hrs	18hrs	21hrs	24hrs	27hrs	30hrs	33hrs	36hrs	39hrs	42hrs	45hrs	48hrs
Indicate time		—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—	—:—
Temperature (36.1 - 38.0°C)	>38°C																			
	37.5-38°C																			
	36-37.4°C																			
	35-35.9°C																			
	<35°C																			
Respiratory rate (12-20 per minute)	>25																			
	20-25																			
	5-19																			
	<5																			
Blood pressure (Diastolic: 60-80mmHg, Systolic: 90-140mmHg)	>190																			
	180																			
	170																			
	160																			
	150																			
	140																			
	130																			
	120																			
	110																			
	100																			
	90																			
	80																			
	70																			
	60																			
	<50																			
Heart rate (51-90 per minute)	>190																			
	160-189																			
	50-159																			
	<50																			
Oxygen	90-100%																			
	<90%																			
Hydration (please tick)	Well hydrated																			
	Poorly hydrated																			
Side effects (please tick)	No side effects																			
	Signs of side effects																			
Consciousness (please tick)	Asleep + unrousable																			
	Asleep but rousable																			
	Awake + calm																			
	Awake + active																			

Once completed please upload onto RiO.