Sussex Partnership NHS
NHS Foundation Trust

The Rapid Tranquillization Policy.

(The Use of Medication in the Control of Acutely Disturbed or Violent Behaviour).

(This policy applies to Working Age Adult, Secure & Forensic, Specialist Women's, Older People's and Children & Young Peoples Services).

Version 6 – July 2014 (replaces 142/Clinical)

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Executive Summary:

- **When to consider using Rapid Tranquillization and the process to follow, including record keeping, monitoring and training.**
- **Consideration of advance directives.**
- **Specific risk issues.**

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1. Introduction[1]

1.1 Purpose of this Policy.

The purpose of this document is to provide staff working in Sussex Partnership NHS Foundation Trust wards with guidance about the use of Rapid Tranquillization (RT). It sets out the main provisions of appropriate use of RT, use of associated medication and the roles and responsibilities of staff.

1.2 Scope of this Policy.

This document applies to all qualified medical and nursing staff (and non-medical prescribers) involved in the prescribing and/or administration of medication for RT. This includes staff employed by the Trust and also those healthcare staff who are either seconded or contracted to the Trust. The document covers the treatment of inpatients in working age adult services, secure and forensic services, specialist women's services, older people's services and children and young peoples services.

Currently this document does not cover adults with learning disabilities or patients with a primary diagnosis of substance misuse.

1.3 Definition.

Rapid Tranquillization is the use of medication (either oral or parenteral) to calm a patient who is exhibiting acutely disturbed or violent behaviour. It is intended to reduce the risk of harm to the patient and also to other patients and members of staff by reducing agitation and aggression. The optimal delivery of RT will allow further psychiatric evaluation to take place and will not compromise patient comprehension or their ability to respond to spoken messages or instruction.

1.4 Principles.

RT should only be considered once de-escalation and other strategies have failed to calm the patient. (See section 3.4). The intervention (along with physical intervention and seclusion) should be considered a management strategy and not be regarded as a primary treatment technique. When determining which intervention to employ, clinical need, the safety of service users and others and, where possible, any advance directives should always be taken into account. The intervention selected must be a reasonable and proportionate response to the risk posed by the patient at that particular time. The reasons for using RT (and any other intervention) must always be explained to the patient at the earliest opportunity.

1.5 Equality Impact Assessment. **(Undertaken in March 2011).**

All patients covered by this policy, regardless of their race, gender, gender identity, sexuality, religion, spiritual beliefs or disability, will be treated equally within the principles of the policy and with equal dignity and respect.

1.6 Training Expectations.

1.6.1. An understanding of the Rapid Tranquillization Policy is essential for all qualified staff that may be called upon to prescribe and/or administer medication in response to situations described in the Prevention and Management of Violence and Aggression (PMVA) Policy. These two documents should be read in conjunction. Staff must also be familiar with the Trust Resuscitation Policy and the Trust Therapeutic Engagement and Observation Policy.

It is considered essential that all qualified medical and nursing staff working in inpatient units be trained in the use of RT, (based on the treatment algorithm most suitable for their unit), and that this training is undertaken every two years. The responsibility to ensure adequate training is undertaken lies with ward managers and modern matrons (for nursing staff) and with consultants and local tutors (for medical staff).

1.6.2 The training requirement for RT varies according to whether the member of staff is a doctor (or non-medical prescriber) or a nurse.

All new medical staff will receive specific training in RT as part of their induction training. This will be delivered by a senior doctor experienced in the use of RT.

Nursing staff will receive RT training as part of their PMVA training course and receive a further 15-minute briefing as part of their Medicines Management Update day. Ward managers and modern matrons will ensure that each member of their nursing staff receives sufficient training in the use of RT and in the use of the treatment algorithm(s) appropriate to their care group. Newly qualified staff will also be expected to pass the RT competencies as outlined in the Trust Preceptorship Policy.

Wherever possible, RT training will be accessed within three months of commencing an inpatient role. Ward managers and modern matrons will keep updated records of their staff that have completed this training and the Trust central training department must be informed of staff completing the training on a monthly basis.

Training will cover the properties of benzodiazepines, the benzodiazepine antagonist flumazenil, antipsychotics, antimuscarinics and antihistamines, their doses and how they are used in the RT process. It will also cover associated risks, including cardio-respiratory effects in response to acute administration of the drugs, particularly when the patient is highly aroused and may have been misusing drugs, is dehydrated or is possibly physically ill.

All staff involved in RT also need to be adequately trained in the maintenance of patient's airways, cardio-pulmonary resuscitation (CPR), the use of defibrillators and the use of pulse oximeters.

1.6.3 A 45-minute PowerPoint presentation is available on the medication section of the Trust website and contains all the necessary information for training clinical staff in use of RT. It can be used in large group or local training sessions and can be incorporated into wider PMVA training programmes. Wherever possible, this presentation should be delivered by a senior nurse or doctor experienced in the use of RT. The pharmacy team will also be available to give support and advice whenever possible. Time for discussion should be included in any training package and therefore the period allowed for specific training on RT, whether independent or as part of another training package, should not be less than one hour.

1.6.4 In addition, the pharmacy team delivers a 15-minute update in their Medicines Management Essential Training Day for Qualified Nurses. This includes advising nurses of any significant changes to policy or practice that have occurred since they had their original training in RT. However, this update cannot be treated as a substitute for the more comprehensive training session.

2. Policy Statement.

The Trust recognises that, at times, some of the patients with whom it works may respond to their feelings of aggression or extreme agitation. Therefore, it is important that Trust staff are appropriately trained and supported in order to ensure the safe administration of oral and/or parenteral medication and the monitoring of its effects on the patient.

When a decision needs to be made on behalf of a patient, staff will make this decision in accordance with the principles of best interest and least restrictive option. (See also section 3.2 for Mental Health Act considerations).

3. Policy and Procedural Practice.

3.1 Key Priorities.

3.1.1 Resuscitation facilities must be available within 3 minutes in all healthcare settings where RT might be used. Equipment available must include an automatic external defibrillator, a bag valve mask, oxygen and suction equipment. All equipment must be properly maintained and checked on a weekly basis and a record maintained.

3.1.2 All prescribers and staff involved in RT must be familiar with and have access to the Trust Resuscitation Policy.

3.1.3 All staff involved in an incident requiring the use of parenteral RT (or physical intervention) should be aware of the potential for damage to the patient / professional relationship and ensure that everything possible is done to avoid its impact.

3.1.4 Any incident requiring parenteral RT (or physical intervention or seclusion) must be contemporaneously recorded. All appropriate staff should be trained to ensure that they are aware of how to correctly

record any incident using the appropriate documentation (IR1).

3.1.5 Where possible a post-incident review should take place as soon as possible and within 72 hours of an incident ending. This review should be lead by the Ward Manager (or nominated deputy) and address the following factors:

- What happened during the incident? What were the trigger factors?
- Each person's role in the incident.
- Their feelings at the time of the incident, at the review and how they may feel in the near future.
- What can be done to address their concerns?

3.1.6 All staff involved in RT need to be aware of the legal framework that authorises this intervention. The intervention should be in line with the guidance contained within the current Mental Health Act code of practice, (and the Mental Capacity Act), and any departure from that guidance should be clearly recorded and justified as being in the best interests of the patient. (See section 3.2)

3.1.8 **Specific to ChYPS**. All patients must be informed that medication is to be given and given the opportunity at any stage to accept oral medication voluntarily. In children/adolescents who are not Gillick competent, parent(s)/carer(s) should be informed of the situation and consent sought for treatment, in advance if at all possible. It is good practice to inform the child/adolescent and parent(s)/carer(s). Consent forms are available from the Trust website.
http://www.sussexpartnership.nhs.uk/services-and-information/medication/professionals/documents/medication-related-charts-and-forms/

3.2 Mental Health Act Considerations.

3.2.1 Patients detained under the treatment sections of the Mental Health Act are subject to Consent to Treatment provisions of Part 4 of the Act. If a patient has been detained for more than 3 months their consent, or authorisation for treatment from a Second Opinion Appointed Doctor (SOAD), is required under Section 58(3) including the completion of statutory forms T2 or T3 before treatment can be given, unless the patient meets the criteria for treatment under Section 62 – urgent treatment.

3.2.2 If the patient has been subject to the Act for less than 3 months, treatment can be given under the provision of Section 63.

3.2.3 All information relevant to MHA status must be fully documented in the clinical record.

3.2.4 The patient's legal status should be reviewed whenever parenteral medication is considered. The enforced administration of medication by injection to an informal patient may necessitate use of the Mental Health Act. If treatment is to continue against the patient's wishes then

a MHA assessment must be undertaken to ensure continued administration is lawful.

3.3 Rapid Tranquillization and Seclusion

A combination of these two interventions is not absolutely contra-indicated providing that the following points are established:

- If the patient is secluded, potential complications in response to RT are particularly serious and must be given full consideration.
- The patient must be monitored by “within eyesight” observation. (See also the Trust Therapeutic Engagement and the Trust Observation Policy and Seclusion Policy).
- Seclusion should be ended when RT has taken effect.

3.4 OVERVIEW OF THE SHORT-TERM MANAGEMENT OF DISTURBED / VIOLENT BEHAVIOUR[1]

PREDICTION
Risk assessment
Necessary & Lawful Searches
Mental Health Presentation
Behavioural Presentation
Other incidents (especially if escalating).

↓

PREVENTION
De-escalation techniques
Observation

↓

INTERVENTIONS FOR CONTINUED MANAGEMENT
Consider, in addition to above, one or more of the following:

Rapid Tranquillization (RT)	Seclusion	Physical Intervention
Use to avoid prolonged physical intervention Medication is required to calm a psychotic or non-psychotic behaviourally disturbed service user	Used to avoid prolonged physical intervention	Better if service user responds quickly Can be used to facilitate administration of RT and/or to enable RT to take effect
CONTRA-INDICATED AS AN INTERVENTION		
When service user has taken previous medication	Should be terminated when rapid tranquillization, if given, has taken effect When other interventions not yet explored	Prolonged physical intervention

↓

POST-INCIDENT REVIEW

Continuous risk reassessment and use of de-escalation techniques

4 Medication

4.1 Treatment aims[2]

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

4.2 Prescribing

4.2.1 Only a Trust prescriber should prescribe medication for RT. The reason for prescribing should be documented in the clinical record, including the treatment plan.

4.2.2 Prescribing of the medication should take into account any contra-indications, warning or precautions required [4]. For instance, patients with co-existing physical illness (especially liver, renal or/and cardiac impairment) and/or patients taking other prescribed medicines, alcohol or illicit drugs, should have drug and dose adjusted as necessary. Patients with a history of, or risk factors for, seizures should have antipsychotics prescribed cautiously, as antipsychotics lower seizure threshold.

4.2.3 Caution is required in patients who are pregnant or believed to be pregnant or if a patient is breast-feeding. Drug choice and dosage are dependent on potential benefit to the patient and potential risk to the foetus.

4.2.4 Full details of contra-indications, special warnings and precautions for all medicines can be found on http://www.medicines.org.uk/emc

4.3 Choice of medication

4.3.1 Where practicable, oral RT medication should always be offered to the patient in the first instance, before considering use of parenteral medication. (See algorithms 1, 2 and 3).

4.3.2 If an advance directive has been completed this should be considered in the first instance. If for clinical reasons an advance directive is not followed, the doctor should fully record these reasons in the patient's clinical record. Patient preference for medication should also be considered at this stage.

4.3.3 It should be noted that antipsychotics in RT are not used for their antipsychotic action as onset of the antipsychotic effect can take several weeks.

4.3.4 It is important to note that medications within the CAMHS algorithm (see algorithm 3) include unlicensed use of medications:

- Olanzapine (oral and IM) is unlicensed for use in patients aged less than 18 years.
- Lorazepam (oral and IM) is unlicensed for use in patients aged less than 12 years.

4.4 High doses. (See appendix 5)**.**

In certain circumstances, current British National Formulary (BNF) doses and limits, and the manufacturers Summary of Product Characteristics (SPC), may be knowingly exceeded e.g. in the case of lorazepam. This decision should not be taken lightly or the risks underestimated, and a risk-benefit analysis should be recorded in the clinical record and a rationale in the care plan. Where the risk-benefit is unclear, consideration should be given to seeking advice from clinicians who are not directly involved in the care of the patient.

If current BNF or SPC doses are exceeded it is particularly important to undertake frequent and intensive monitoring of a calmed patient. Particular attention must be given to regular checks of the airway, level of consciousness, pulse, blood pressure, respiratory effort, temperature and hydration. If the patient is not amendable to monitoring of their vital signs an observation record should be made of their level of consciousness, physical activity, mobility, skin colour and breathing.

5 Administration of medication

5.1 See Appendix 5 for drug specific details of administration.

5.2 Any medication administered must be clearly and fully documented on the Drug Prescription and Administration Record Chart. The patient's response to the medication must be clearly and fully documented in their clinical record with clear reference made to the use of medication for Rapid Tranquillization purposes.

5.3 Medicines for injection must not be mixed in the same syringe.

5.4 Whilst it is recognised that intramuscular (IM) injections may need to be administered to a resisting / struggling patient, extreme care must be taken with the injection as in these cases there is a greater risk of hitting a vein and the drug being given intravenously (IV).

5.5 Nursing and medical staff should always have a short feedback session following emergency restraint and RT.

5.6 Following RT, discussion should always be held with the patient and their views sought on the episode. This should be documented in their clinical notes and they should be offered the opportunity to write their own account.[1] Consideration must be given to providing appropriate assistance to those patients who do not use English as their first language and those who may have other communication difficulties due to age or disability.

6 Monitoring the patient and recording.

6.1. If possible, baseline measurements of the following should be recorded before any parenteral drug administration:

- Temperature
- Pulse and respiration rate
- Blood pressure

If these cannot be done, reference should be made to any recently obtained baseline measurements that are available. In such circumstances there should be a record made of what can be observed, for example, evidence of injuries, level of consciousness, pallor, breathing and mobility. If no physical observations can be made a record should still be made in the clinical notes of the reason for this and the fact that the patient was still monitored.

6.2 Where possible, (and where it is safe to do so), temperature, pulse, respiration rate and blood pressure should be recorded at least every 10 minutes for the first hour following the parenteral administration of any drug. Thereafter, they should be recorded at half-hourly intervals until the patient is fully ambulatory.

6.3 The record of TPR and blood pressure must be made on physical health monitoring form normally used by the unit and be filed in the patient's clinical notes upon completion.

6.4 All patients administered RT must be subject to either **intermittent, arms-length or within eyesight observation, according to assessed clinical need.** Assessment must take into consideration the patients physical health status as well as their current psychiatric presentation and the assessment and rationale for the level of observation must be clearly recorded in the clinical notes. Observations must continue for at least one hour and until the patient is assessed as being calm and any changes to physical health parameters have returned to normal. The level of observation required should also be reassessed and any change recorded throughout the episode. Wherever possible, staff should ensure the patient remains adequately hydrated during the episode. In addition, staff should closely monitor for signs of extrapyramidal side effects (and in particular, laryngeal dystonia) in response to the administration of antipsychotic medication, by any route.

6.5 Where the patient is unconscious or asleep, the same monitoring should take place so far as is possible, and pulse-oximetry should also be used, where it is practical to do so.

6.6 Where possible, and where facilities exist, ECG and haematological monitoring are strongly recommended whenever antipsychotics are administered and especially where high doses or parenteral route are be used. High stress levels, restraint, agitation, and hypokalaemia all place the patient at high risk of developing cardiac arrhythmias.
The RT event should always be fully recorded in the clinical notes.

7 Medication Specific Risks

There are specific risks with different classes of medication and these risks may be compounded when medication is used in combination. Close monitoring of the patient is essential.

Benzodiazepines	Loss of consciousness, respiratory depression or arrest, cardiovascular collapse (particularly in patients already receiving clozapine), disinhibition. Note: midazolam carries a higher risk than lorazepam of causing respiratory depression. Particular caution should be exercised if considering use of midazolam in elderly, frail or physically unwell patients.
Antipsychotics	Loss of consciousness, cardiovascular / respiratory complications and collapse, seizures, akathisia, dystonia, dyskinesia, neuroleptic malignant syndrome, excessive sedation.
Antihistamines	Excessive sedation, painful injection and additional antimuscarinic effects.

8 Discontinuation of Rapid Tranquillization

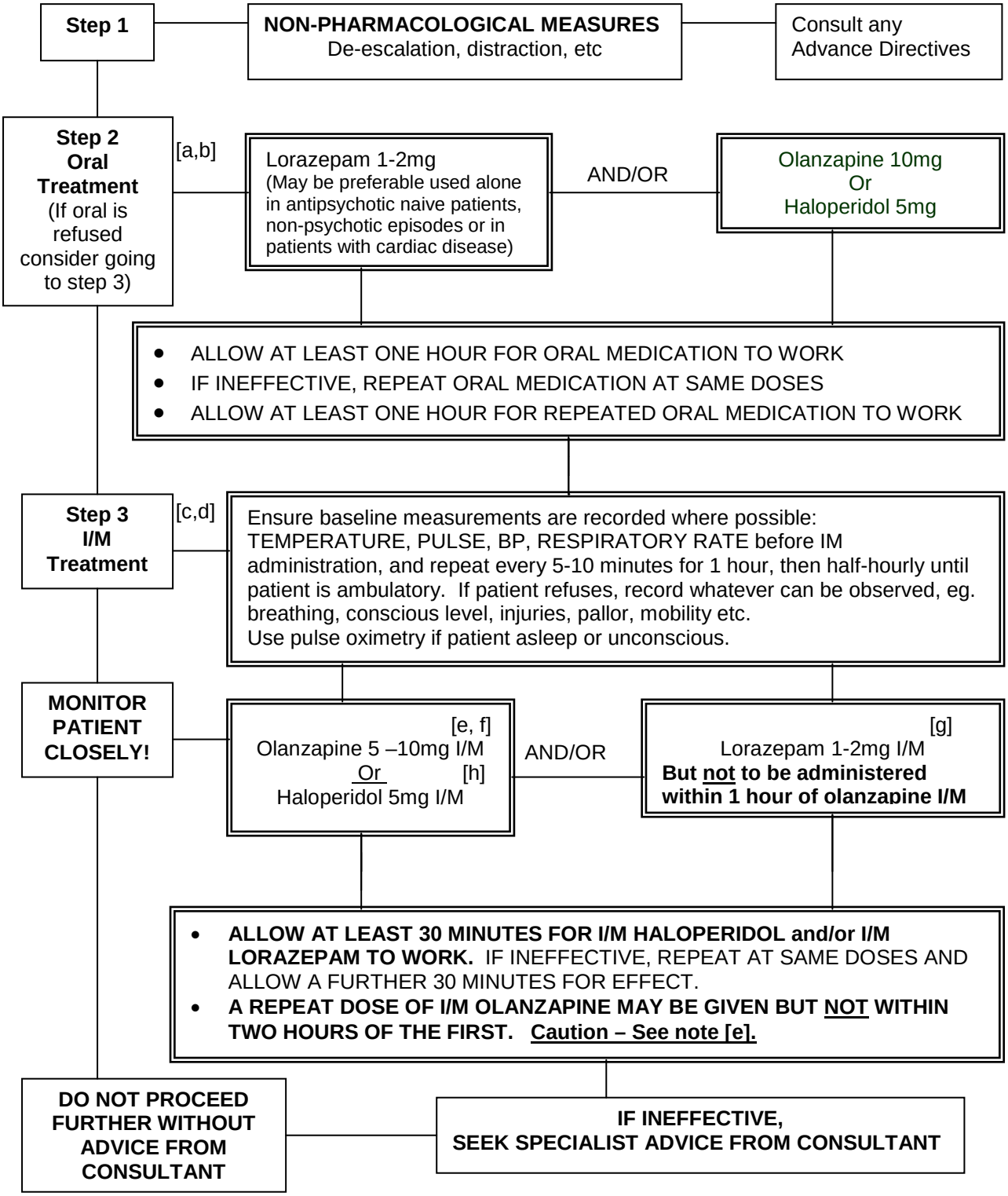
RT should be discontinued at the point of response. Thereafter, the patient must continue to be closely monitored, and future medication (both regular and as required) should be reviewed.

9 Advance Directives

Once a patient has received RT, consideration should be given to drawing up an advance directive for future occasions. This should take into account the response to medication and the patient's experience of the event. (See section 3.1.6).

Algorithm 1.

Rapid Tranquillization of the Acutely Disturbed / Violent Patient
- Working Age Adult -



[a, b, c, d, e, f, g, h – see notes].

Notes:

a. Choice depends on current treatment.
- If patient is established on antipsychotics, lorazepam may be used alone.
- If the patient uses 'street drugs' or already receives regular benzodiazepines, an antipsychotic may be used alone.
- For the majority of patients who are not antipsychotic naive, best response will be with combination therapy.

a. Ensure procyclidine injection is available. Antipsychotic may cause acute dystonic reaction.

b. As in (a), either antipsychotic or benzodiazepine may be used alone, but best results are likely with combination therapy.

c. Ensure flumazenil injection is available to reverse effects of lorazepam (or midazolam) injection.

d. The maximum dose of olanzapine is 20mg/24 hours by any (combined) route(s) – this should not be exceeded without obtaining specialist advice – and not more than 3 I/M doses may be given in any 24-hour period. **Intramuscular olanzapine and intramuscular lorazepam must not be administered within 1 hour of each other.**

e. Olanzapine IM needs to be diluted before administration in 2.1ml water for injection. It is stable for up to 1 hour after reconstitution. The following table provides injection volumes for delivering various doses of olanzapine:

Dose (mg)	Volume of Injection (ml)
10	2.0
7.5	1.5
5	1.0
2.5	0.5

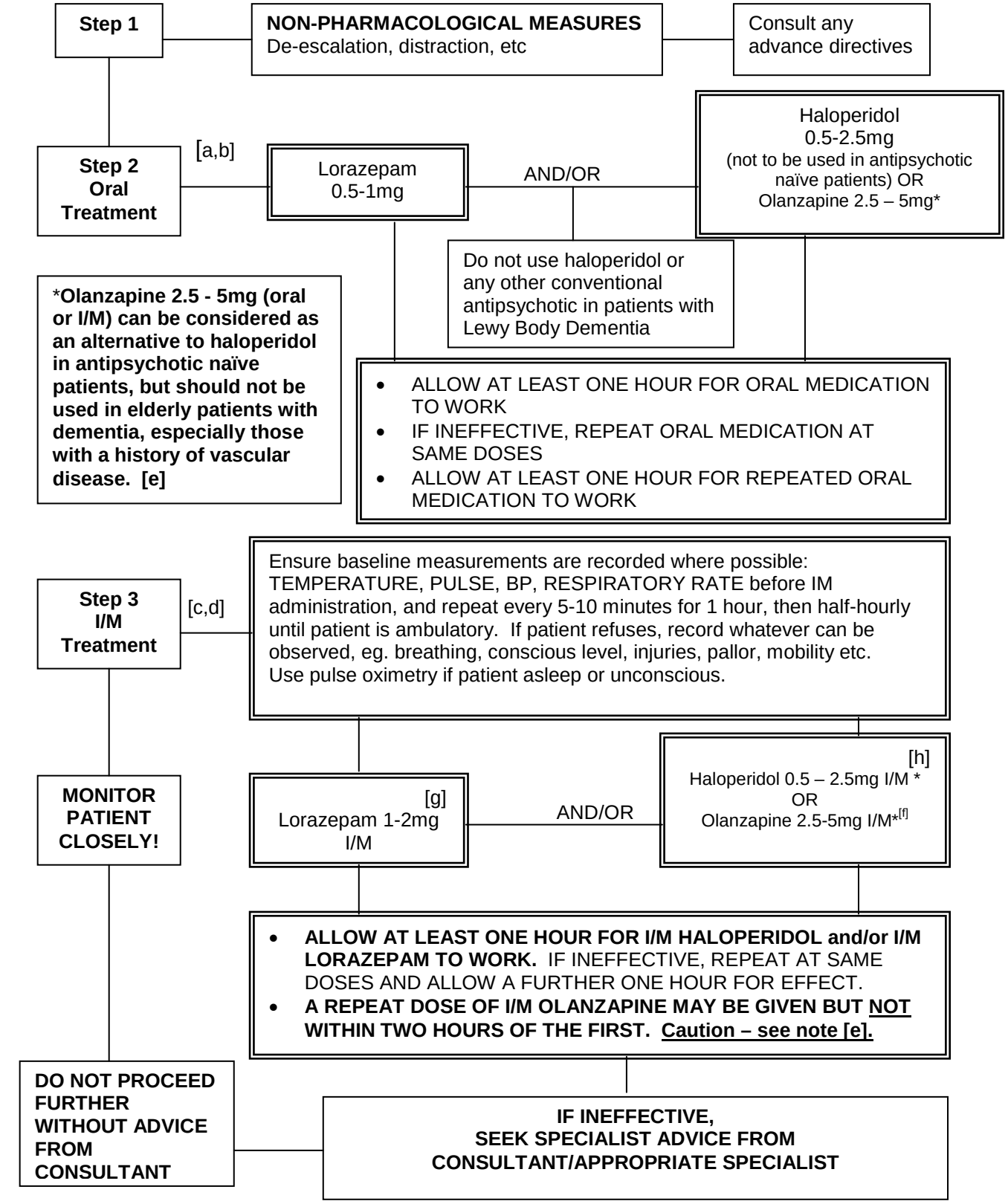
f. Lorazepam should be mixed 1:1 with water before injecting. The following table provides injection volumes for delivering various doses of lorazepam **once diluted**.

Dose (mg)	Volume of Injection (ml)
4	2.0
3	1.5
2	1.0
1	0.5

g. The maximum daily dose of haloperidol is either 20mg orally or 12mg by intramuscular injection. Maximum doses will need to be adjusted if a combination of both routes is used. The bioavailable equivalence of haloperidol being approximately 10mg oral: 6mg intramuscular.

Algorithm 2.

Rapid Tranquillization of the Acutely Disturbed / Violent Patient
- Patient Aged Over 65 Years – (not for routine management of delirium)



[a, b, c, d, e, f, g, h – see notes].

Notes:

b. Choice depends on current treatment.
- If patient is established on antipsychotics, lorazepam may be used alone.
- If the patient uses 'street drugs' or already receives regular benzodiazepines, an antipsychotic may be used alone.
- For the majority of patients who are not antipsychotic naive, best response will be with combination therapy.

c. Ensure procyclidine injection is available. Antipsychotic may cause acute dystonic reaction.

d. As in (a), either antipsychotic or benzodiazepine may be used alone, but best results are likely with combination therapy in patients who are not antipsychotic naive.

e. Ensure flumazenil injection is available to reverse effects of lorazepam (or midazolam) injection.

f. The maximum dose of olanzapine is 20mg/24 hours by any (combined) route(s) – this should not be exceeded without obtaining specialist advice – and not more than 3 I/M doses may be given in any 24-hour period. **Intramuscular olanzapine and intramuscular lorazepam must not be administered within 1 hour of each other.**

g. Olanzapine IM needs to be diluted before administration in 2.1ml water for injection. It is stable for up to 1 hour after reconstitution. The following table provides injection volumes for delivering various doses of olanzapine:

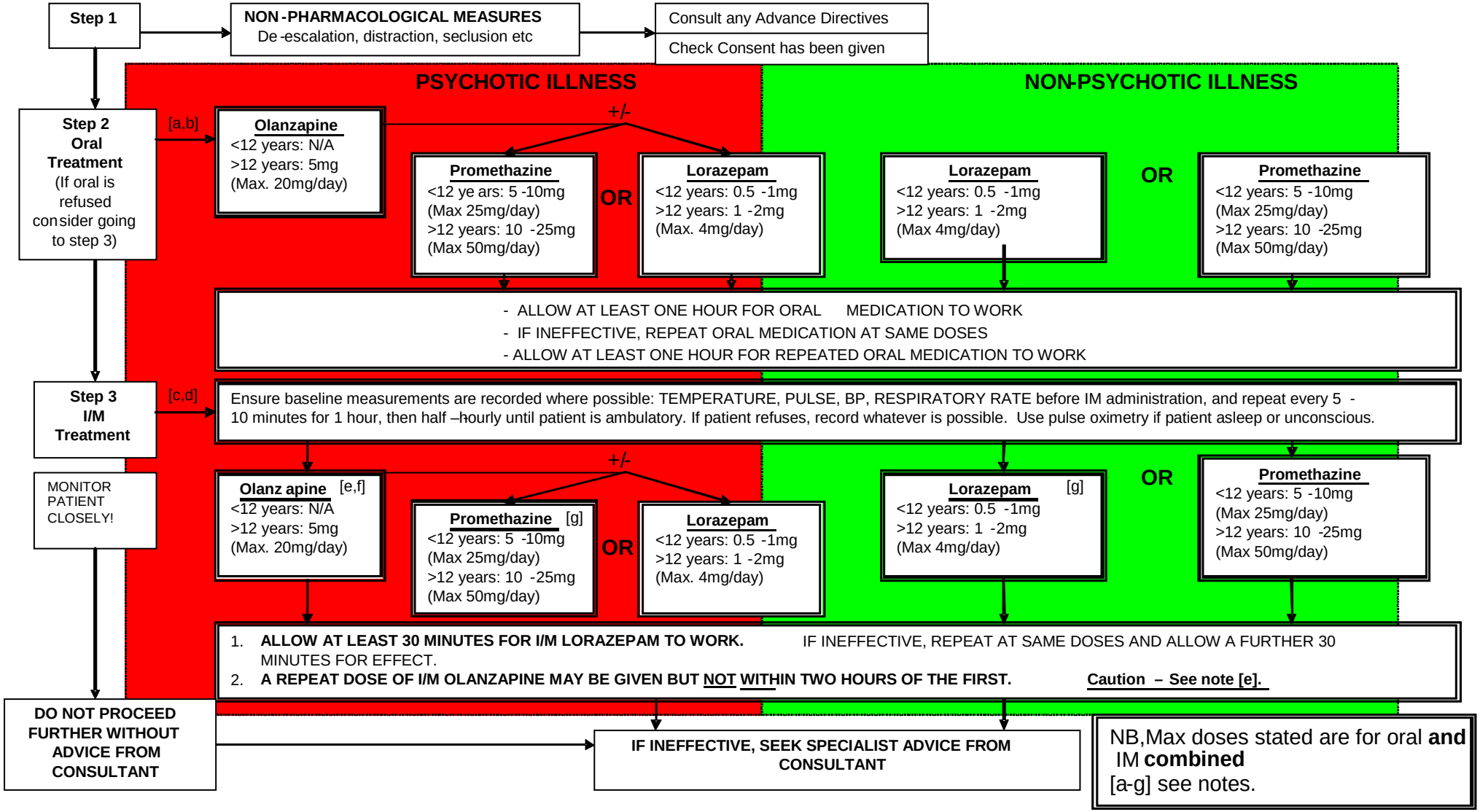
Dose (mg)	Volume of Injection (ml)
10	2.0
7.5	1.5
5	1.0
2.5	0.5

h. Lorazepam should be mixed 1:1 with water before injecting. The following table provides injection volumes for delivering various doses of lorazepam **once diluted**.

Dose (mg)	Volume of Injection (ml)
4	2.0
3	1.5
2	1.0
1	0.5

i. The maximum daily dose of haloperidol is either 10mg orally or 6mg by intramuscular injection. Maximum doses will need to be adjusted if a combination of both routes is used. The bioavailable equivalence of haloperidol being approximately 10mg oral: 6mg intramuscular.

Algorithm 3. Rapid Tranquillization of the Acutely Disturbed / Violent Patient - Children and Adolescents Aged 6 to 17 Years



Notes:

a. Choice depends on current treatment.
   - If patient is established on antipsychotics, lorazepam may be used alone.
   - If the patient uses 'street drugs' or already receives regular benzodiazepines, an antipsychotic may be used alone.
   - For the majority of patients who are not antipsychotic naive, best response will be with combination therapy.
   - Promethazine may be useful for patients who develop disinhibition as a result of benzodiazepine use.

b. Ensure procyclidine injection is available. Antipsychotic may cause acute dystonic reaction.

c. As in (a), either antipsychotic, benzodiazepine or promethazine may be used alone. Promethazine may be useful for patients who develop disinhibition with benzodiazepine use.

d. Ensure flumazenil injection is available to reverse effects of lorazepam injection.

e. The maximum dose of olanzapine is 20mg/24 hours by any (combined) route(s) – this should not be exceeded without obtaining specialist advice – and not more than 3 I/M doses may be given in any 24-hour period. **Intramuscular olanzapine and intramuscular lorazepam must not be administered within 1 hour of each other.**

f. Olanzapine IM needs to be diluted before administration in 2.1ml water for injection. It is stable for up to 1 hour after reconstitution. The following table provides injection volumes for delivering various doses of olanzapine:

Dose (mg)	Volume of Injection (ml)
10	2.0
7.5	1.5
5	1.0
2.5	0.5

g. Lorazepam should be mixed 1:1 with water before injecting. The following table provides injection volumes for delivering various doses of lorazepam **once diluted**:

Dose (mg)	Volume of Injection (ml)
4	2.0
3	1.5
2	1.0
1	0.5

10 Specialist Advice for Working Outside the Appropriate Algorithm

(NB. Recommended adult doses are quoted. Doses will usually be lower in the elderly and in children and young people).

10.1 Advice must be sought from the consultant or appropriate specialist, at any stage of RT if any doubt exists regarding how best to proceed or if the treatment algorithms have been followed and there is no improvement.

10.2 Physical illness should be re-investigated.

10.3 The following treatments are rarely used, have a minimal evidence base and are unlicensed. **They may only be prescribed by a consultant psychiatrist or appropriate specialist who has previous experience of their use.** Any decision to use these treatments must only be taken when more conventional treatments have failed and the reason for use must be fully documented in the patient's notes. The advice below relates to use in adults.

10.3.1 Promethazine 50mg PO or IM may be useful in benzodiazepine-intolerant patients or when an increase in seizure threshold could be problematic, for instance in the case of emergency ECT. (See 10.5). Promethazine may be useful in children and adolescents who may be at increased risk of disinhibition with benzodiazepines. Promethazine can cause a postural drop in blood pressure therefore when given IM it should not be given at the same time as olanzapine - wait 1 hour between them. (See Appendix 6).

10.3.2 Levomepromazine 12.5-50mg IM is highly sedative. Avoid in adults over 50 years due to significant hypotensive effects. Avoid in children and adolescents.

10.3.3 Risperidone 1-2mg orally with or without lorazepam. Repeat at one hour intervals.

10.3.4 Quetiapine 50-100mg orally may be considered as per use for acute mania.

10.3.5 **Acuphase® (zuclopenthixol acetate) should not be used routinely in the RT setting** (See appendix 3) and is not appropriate for use in antipsychotic naïve patients. It should only be used in situations where patients refuse oral medication and require frequent IM injections. However if Acuphase® is appropriate medication for a known patient and this is documented in the notes it may be included in rapid tranquillization under an advanced directive.

10.3.6 IM midazolam can no longer be considered due to the relatively high risk of respiratory depression with this product. Further to this, and in response to the Department of Health's *Never Events List 2012/13* (published January 2012), the Trust Drugs & Therapeutics Group took the decision in January 2013 that this product would no longer be made available to Trust units.

10.4 If prescribing more than one antipsychotic or prescribing in excess of maximum doses, (see Appendix 5), an ECG should be carried out to exclude arrhythmias.

10.5 Emergency ECT may also be considered but only by a specialist.

11 Intravenous Therapy.

11.1 The intravenous administration of benzodiazepines or haloperidol should not normally be used other than in very exceptional circumstances, which should be specified and recorded. This decision should only be taken by a consultant or appropriate specialist who has previous experience of using intravenous interventions. Administration may only be undertaken by a practitioner who is fully trained in IV administration.

11.2 If immediate tranquillization is essential then intravenous administration may be considered necessary. If so, it is essential that attending staff have been appropriately trained to recognise symptoms of respiratory depression, acute dystonia and cardiovascular compromise.

11.3 If intravenous medication is used, the patient **must be subject to within eyesight observation**. Intravenous administration must not take place without full access to support and resuscitation services. (See Trust Resuscitation Policy).

12 Responsibilities.

Healthcare organisations have an obligation to ensure treatments are safe and effective and to ensure their staff receive appropriate training. This section aims to help staff understand their responsibilities and accountabilities, it is not exhaustive and professionals must also consider their own Codes of Practice.

12.1 The Trust:

Will ensure that Governance arrangements are in place and will include audit procedures that relate to training needs and provision, and the review of untoward incidents.

Will ensure that that the policy is reviewed and updated to support Governance arrangements.

Will ensure that the policy is current and based on national guidance.

Will learn and react appropriately to any untoward incidents and events related to RT.

Will respond or react to any resource implications related to RT.

12.2 Medical and Nursing Professional Leads:

Will provide or facilitate the provision of training required to support the clinical principles of this policy.

12.3 Trust Pharmacy Team:

Will provide 15-minute updates on RT as part of the Medicines Management essential training day for qualified nursing staff.

Will offer advice with regard to the content of more comprehensive training and with regard to any changes of policy or guidance that may be needed due to amended national guidance on the use of RT medication.

12.4 Ward Managers and Modern Matrons:

Will understand the policy requirements as it relates to their areas of service and be responsible for the implementation of the policy within their scope of management.

Will identify and support the RT training needs of their nursing staff through preceptorship and supervision programs, staff appraisal and the PDP process, and will reflect these in service training plans.

Will identify and manage service needs in relation to training, skill mix and staff availability to ensure safe procedures for RT at all times.

Will ensure that all registered nurses working in inpatient units and PICUs receive RT training or updates at least every two years.

Will ensure that RT medication and other associated medication is available and regularly checked to ensure nothing is missing and nothing is due to expire.

Will ensure supportive measures are available to all staff following an RT incident and will ensure that time is made available for reflection and exploration of learning points.

12.5 Consultants:

Will understand the policy requirements as it relates to their areas of service and be responsible for the implementation of the policy within their scope of management.

Will liaise with local tutors to identify and support the RT training needs of their junior grade doctors through training programs, supervision, appraisal and the PDP process, and will reflect these in staff training plans.

12.6 Individual Clinical Staff:

Will read and understand the policy and guidance.

Will identify their own training needs in relation to RT through the appraisal process, with reference to the Trust essential training policy.

Will only carry out RT procedures that they have been trained and assessed as competent to do.

13 Monitoring Compliance with the Policy.

The Drugs and Therapeutics Group will ensure that audits are carried out against the standards set by this policy and guidance.

In conjunction with the audit feedback, this policy will be reviewed at least bi-annually to embed any identified improvements, changes in legislation or best practice. The review will be undertaken by the Chief Pharmacist (Governance & Professional Practice) and will be supported by the Executive Sponsor.

The assistance of the Clinical Audit department will be sought for specific audits.

This policy will be updated on a regular basis to ensure that it continues to reflect national guidance and the NHSLA Risk Management Standards.

14 Development, consultation and ratification.

This Trustwide policy and guidance was originally developed by the Trust pharmacy team in 2008. Wide consultation and development involved the following forums and individuals. A pro-forma was issued to capture feedback.

- **Trust Drugs & Therapeutics Group**
- **Trust Pharmacy Forum**
- **Trust Health and Safety Committee**
- **Trust Associate Directors of Nursing**

The policy was originally ratified by the Trust Professional Practice Forum (PPF) in October 2008. At this point the policy did not cover the use of Rapid Tranquillization in Child and Adolescent Services.

In 2009 the policy was extended to cover the use of Rapid Tranquillization in CAMHS. This work was undertaken by the Trust's specialist clinical pharmacist for CAMHS in liaison with CAMHS consultants. The extension to the policy was approved by the Drugs & Therapeutics Group in October 2009.

The policy received further review with regard to patient monitoring procedures and staff group responsibilities, by a working group of consultants, senior nurses and pharmacists between November 2010 and March 2011. Amendments were approved by the Drugs & Therapeutics Group in April 2011.

15 Dissemination and Implementation of policy.

Following ratification of this policy the Executive Sponsor will ensure the document is forwarded to the Health & Social Care Governance Support Team who will allocate an official document number and log the document on the Trust central database The HSCG Support Team will inform the sponsor and document authors of the official document number allocated.

The Chief Pharmacists will ensure that the policy is posted on the Trust website and that further staff notification occurs via the D&T Newsletter.

Further dissemination will be agreed between the authors and the Executive Sponsor and compliance against specified training will be monitored through the audit process.

16 Document Control including Archive Arrangements.

The Health & Social Care Governance Support Team will maintain an archive of previous versions of the policy and will update the central database and website. Archived documents will be listed on the database, with details of the date they were archived and removed from the website and a link to the superseding document if appropriate.

Requests from staff to access archived procedural documents can made to the Health & Social Care Governance Support Team (for all documents dated April 2006 onwards). Requests from other organisations or individuals outside of the Trust must be made in accordance with the Freedom of Information Act.

17 References.

1) Violence – the short-term management of disturbed/violent behaviour in psychiatric in-patient settings and emergency departments. National Institute for Clinical Excellence, February 2005.

2) Prescribing Guidelines 9th Edition, 2007. The South London and Maudsley NHS Trust and Oxleas NHS Trust.

3) Paton C. (2002) benzodiazepines and disinhibition: a review. Psychiatric Bulletin; 26: 460-462.

4) Summaries of Product Characteristics. www.medicines.org.uk (Association of the British Pharmaceutical Industry).

18 Other Trust Policies to be Cross-referenced

This protocol should be read and used in conjunction with the following Trust policies and documents.

- Prevention and Management of Violence and Aggression Policy
- Essential Training Policy and Essential Training Matrix
- Resuscitation and Anaphylaxis Policy
- Resuscitation & Basic Life Support with Defibrillation Essential Training Schedule
- Rapid Tranquillization training programme (for medical and nursing staff) – PowerPoint presentation
- Medicines Management Update for Qualified Nurses - Training Schedule
- Therapeutic Engagement & Observation Policy and Procedure
- Seclusion Policy and Procedure
- Guidance on completing an advance directive for mental health care
- Preceptorship Policy and Procedure

19 Bibliography.

National Institute for Health & Clinical Excellence.
Clinical Guidelines for Schizophrenia. December 2002.

National Institute for Health & Clinical Excellence.
Technology Appraisal Number 43 – Atypical Antipsychotics. June 2002.

Royal College of Psychiatrists.
Consensus statement on high dose antipsychotic medication. May 2006.

Appendix 1 – Physical health monitoring and remedial measures

Rapid Tranquillization – monitoring

If possible, after any parenteral drug administration, monitor the following:

Temperature
Pulse
Blood Pressure
Respiratory Rate

Every 5 – 10 minutes, for one hour, then half-hourly until patient is ambulatory.

If the patient is asleep or **unconscious**, the use of pulse oximetry to continuously measure oxygen saturation is desirable. The patient must remain under **within eyesight observation** at least until they are fully ambulatory again.

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

Remedial measures in rapid tranquillization
Get urgent medical assistance if not already present:

Problem	*Remedial measures*
Acute dystonia (including oculogyric crises)	Give **procyclidine** 5 – 10mg IM
Reduced respiratory rate (<10/min) or oxygen saturation (<90%)	Give **oxygen**; raise legs; ensure patient is not lying face down. Give **flumazenil** if benzodiazepine-induced respiratory depression suspected (see Appendix 2). If induced by any other sedative agent, **ventilate mechanically**.
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**, tilt bed towards head. Monitor closely.
Increased temperature	**Withhold antipsychotics** (risk of NMS and perhaps arrhythmias). Check creatinine kinase urgently.

Appendix 2 – Guidelines for Medical Administration of Intravenous Flumazenil in the Emergency Treatment of Respiratory Depression caused by Administration of a Benzodiazepine.

Guidelines for the use of intravenous flumazenil	
Indication for use	If respiratory rate falls below 10/minute after the administration of lorazepam, midazolam or diazepam.
Contra-indications	Patients with epilepsy who have been receiving long-term benzodiazepines.
Caution	Dose should be carefully titrated in hepatic impairment.
Dose and route	*Initial* **200mcg** *intravenously* over 15 seconds - if required level of consciousness not achieved after 60 seconds then, ***Subsequent dose:*** 100mcg over 10 seconds
NB, Children and adolescents 12-18 years of age as above. Children <12 years of age as 10mcg/kg (max. single dose 200mcg).	
Administration	**Only by practitioners fully trained in IV technique**
Time before dose can be repeated	60 seconds
Maximum dose	**1mg in 24 hours** (one initial dose and eight subsequent doses).
Side effects	Patients may become agitated, anxious or fearful on awakening. Seizures may occur in regular benzodiazepine users.
Management	Side effects usually subside.
Monitoring	
• **What to monitor?**	Respiratory rate
• **How often?**	Continuously until respiratory rate returns to baseline level. Flumazenil has a short half life. Respiratory function may recover then deteriorate again.
Note: If respiratory rate does not return to normal or patient is not alert after initial doses assume sedation due to some other cause.	

Appendix 3 – Guidelines for the use of Clopixol Acuphase®

Clopixol Acuphase® (zuclopenthixol acetate) is not recommended for routine use in RT due to its long onset-time and duration of action. However, it can be considered as an option when it is recognised that the patient will be disturbed/violent over an extended time period and has a past history of a good / timely response. Some patients may want "Acuphase" included in advance directives.

Acuphase® should be used only after an acutely psychotic patient has required repeated injections of short-acting antipsychotic drugs such as haloperidol or olanzapine, or sedative drugs such as lorazepam.

Acuphase® should be given only when enough time has elapsed to assess the full response to previously injected drugs: allow 15 mins after IV injections; 60 mins after IM.

Acuphase® should never be administered:

- In an attempt to "hasten" the antipsychotic effect of other antipsychotic therapy
- To a patient who is physically resistant (risk of intravasation and oil embolus)

Acuphase® should never be used for the following:

- Patients who accept oral medication
- Patients who are neuroleptic naïve
- Patients who are sensitive to EPSE
- Patients who are unconscious
- Patients who are pregnant
- Patients with hepatic or renal impairment
- Patients with cardiac disease

Where possible, Acuphase® should not be administered at the same time as parenteral benzodiazepines or at the same time as other parenteral antipsychotics as this may lead to significant over-sedation that is difficult to reverse. (However, note that the administration of the first-dose of Clopixol Depot at the same time as a last-dose of Acuphase® is covered by the product licence).

Onset and duration of action

Sedative effects usually begin to be seen 2 hours after injection and peak after 12 hours. The effects may last for up to 72 hours. **Note: Acuphase® should only be considered as an adjunct to rapid tranquillization since its onset of action is not rapid.**

Dose

Acuphase® should be given in a dose of 50-150mg, up to a maximum of 400mg over a 2-week period. This maximum duration ensures that a treatment plan is put in place. It does not indicate that there are known harmful effects from more prolonged administration, although such use should be very exceptional. There is no such thing as a "course of Acuphase®". The patient should be assessed before each administration.

Injections should be spaced at least 24 hours apart.

Note: zuclopenthixol acetate has often been widely misused as a sort of "chemical straitjacket". In reality it is a potentially toxic preparation with very little published information to support is use. It should be reserved for those few patients who have a prior history of good response.

Appendix 4.1 – Monitoring of Intramuscular Medication (including olanzapine) in Rapid Tranquillization in Working Aged Adults

Note:
1. When considering the use of intramuscular RT medication, full consideration must first be given to the use (or further use) or oral medication and also whether any oral medication administered has had sufficient time to have a beneficial effect.

2. Consideration should also be given to assessment of the patient using the PANSS-EC assessment scale / scoring matrix. Where this is used, intramuscular administration should generally not occur unless the patient scores at least 20, and at least 5 on one dimension. (Assessment by PANSS-EC scoring should only be undertaken by medical or nursing staff that have been trained in it's use).

General considerations:

- Maximum dose of IM haloperidol is 12mg/24hours
- Maximum dose of IM lorazepam is 30micrograms/kg/hour (approximately 6mg/24hours in women and 8mg/24hours in men)
- Maximum dose of olanzapine (combined routes) is 20mg per 24 hours.
- Assuming no oral olanzapine, olanzapine IM injection is usually given as 5mg, and 10mg doses.
- Repeat doses of olanzapine IM can be given after 2 hours.
- **A maximum of 3 olanzapine injections can be given in 24 hrs.**
- Maximum olanzapine course length is 3 consecutive days.
- **Olanzapine must not be given by the IV or SC route.**
- Lorazepam IM must not be given within one hour of IM olanzapine.
- Where possible, (and where it is safe to do so), monitoring and recording of temperature, pulse, respiration rate and blood pressure should take place at 10 minute intervals for the first hour following administration.
- Pulse oximetry must be used if the patient is asleep or unconscious.
- Procyclidine (oral or IM) may be required to treat acute EPSE.

Appendix 4.2 Monitoring of Intramuscular Medication (including Olanzapine) in Rapid Tranquillization in Adults 65 Years Old and Over.

Note:
1. When considering the use of intramuscular RT medication, full consideration must first be given to the use (or further use) or oral medication and also whether any oral medication administered has had sufficient time to have a beneficial effect.

2. Consideration should also be given to assessment of the patient using the PANSS-EC assessment scale / scoring matrix. Where this is used, intramuscular administration should generally not occur unless the patient scores at least 20, and at least 5 on one dimension. (Assessment by PANSS-EC scoring should only be undertaken by medical or nursing staff that have been trained in it's use).

General considerations:

- Maximum dose of IM haloperidol is 6mg/24hours
- Maximum dose of IM lorazepam is 15micrograms/kg/hour (approximately 3mg/24hours in women and 4mg/24hours in men)
- Maximum dose of olanzapine (combined routes) is 20mg per 24 hours.
- Assuming no oral olanzapine, olanzapine IM injection is usually given as 2.5mg and 5mg doses.
- Repeat doses of the olanzapine IM can be given after 2 hours.
- **A maximum of 3 olanzapine injections can be given in 24 hrs.**
- Maximum olanzapine course length is 3 consecutive days.
- **Olanzapine must not to be given by the IV or SC route.**
- Where possible, (and where it is safe to do so), monitoring and recording of temperature, pulse, respiration rate and blood pressure should take place at 10 minute intervals for the first hour following administration.
- Pulse oximetry must be used if the patient is asleep or unconscious.
- Procyclidine (oral or IM) may be required to treat acute EPSE

Appendix 4.3 – Monitoring of Intramuscular Medication (including olanzapine) in Rapid Tranquillization in Children and Adolescents.

Note:
1. When considering the use of intramuscular RT medication, full consideration must first be given to the use (or further use) or oral medication and also whether any oral medication administered has had sufficient time to have a beneficial effect.

2. Consideration should also be given to assessment of the patient using the PANSS-EC assessment scale / scoring matrix. Where this is used, intramuscular administration should generally not occur unless the patient scores at least 20, and at least 5 on one dimension. (Assessment by PANSS-EC scoring should only be undertaken by medical or nursing staff that have been trained in it's use).

General considerations:

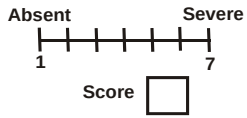
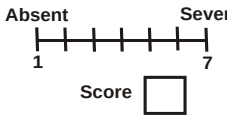
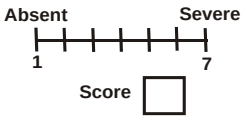
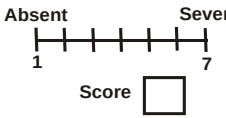
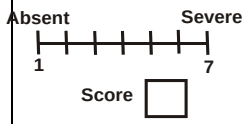
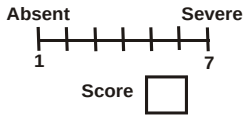
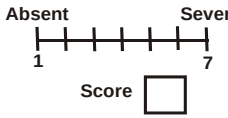
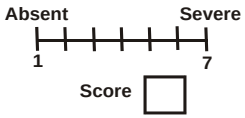
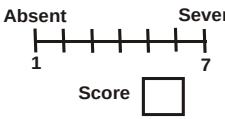
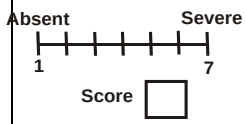
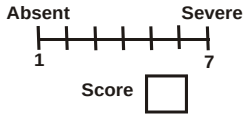
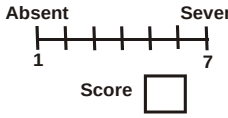
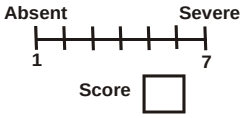
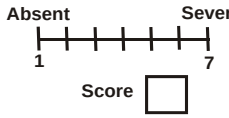
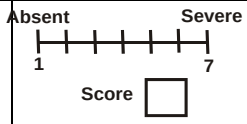
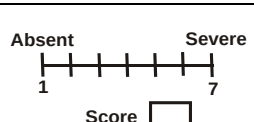
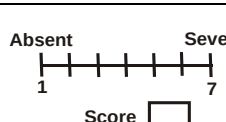
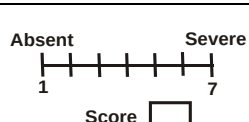
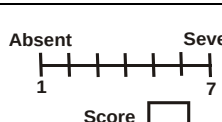
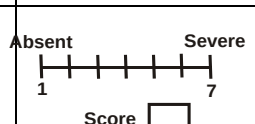
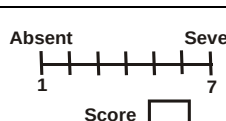
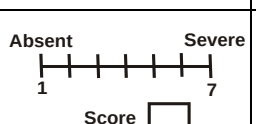
- Maximum dose of IM lorazepam is 4mg for children and adolescents. Use is unlicensed in children under 12 years of age.
- Maximum dose of olanzapine (combined routes) is 20mg per 24 hours. Recommended for use in children and adolescents over 12 years of age. Use is unlicensed (by any route) in children and adolescents under 18 years of age.
- Assuming no oral olanzapine, olanzapine IM injection is usually given as 5mg and 10mg doses. (See note above).
- Repeat doses of the olanzapine IM can be given after 2 hours.
- **A maximum of 3 olanzapine injections can be given in 24 hrs.**
- Maximum olanzapine course length is 3 consecutive days.
- **Olanzapine must not be given by the IV or SC route.**
- Lorazepam IM must not be given within one hour of IM olanzapine.
- Where possible, (and where it is safe to do so), monitoring and recording of temperature, pulse, respiration rate and blood pressure should take place at 10 minute intervals for the first hour following administration.
- Pulse oximetry must be used if the patient is asleep or unconscious.
- Procyclidine (oral or IM) may be required to treat acute EPSE

Appendix 5.

PANSS-EC Scoring Matrix

When scoring use the visual scale first before rounding the score to the nearest whole number

Patient's name: **DoB:** **Ward:** **Date:** **Time of first assessment:**

Dimension → Time	Poor impulse Control	Tension	Hostility	Uncooperativeness	Excitement	Total Score
↓ Zero						
One Hour						
Four Hours						
……. Hours						
……. Hours						

Initial assessment completed by ..... (Signature) ……. (Name in block letters)

Comments and Observations on the PANSS-EC Scoring Matrix

Zero		
One Hour		
Four Hours		
…… Hours		
…… Hours		

Appendix 6

Guidelines for the use of intramuscular promethazine injection – when lorazepam injection is not available, contraindicated or ineffective.

1. **In working age adults, (and in adolescents aged 16 years and over), the recommended dose is 25mg to 50mg. The lower dose should normally be used initially and titrated upwards according to response if necessary. Repeat doses should not be considered within an hour of a previous dose and a maximum dose of 100mg in 24 hours should not be exceeded. Doses of up to 150mg have been used but this would be unlicensed use.**
2. **In the elderly, (and in physically debilitated patients and those with impaired renal, hepatic, cardiac or respiratory function), there are no specific dose recommendations but lower doses should be considered and particular caution should be exercised in patients with a diagnosis of dementia.**
3. **In children and adolescents, younger than 12 years of age the recommended dose is 5-10mg (max 25mg/day). In those older than 12 years of age the recommended dose is 10-25mg (max 50mg/day). The product must not be used in children under 2 years of age.**

Additional Notes.

1. Promethazine intramuscular injection is not licensed for the acute management of disturbed/violent behaviour. However, there are some studies (TREC trails) to support its use in this therapy area.
2. Promethazine injection should not be administered at the same time or within an hour of olanzapine injection due to risk of postural drops.
3. Promethazine has anticholinergic side effects such as dry mouth, blurred vision, urinary retention and constipation. Cognition can also be impaired particularly in patients with a diagnosis of dementia. It should therefore be used with caution in this patient group.
4. Promethazine can also cause EPSE. However, when given with haloperidol these effects were less than those seen with haloperidol alone. (TREC trials)[#]

[#] http://summaries.cochrane.org/CD005146/haloperidol-plus-promethazine-for-psychosis-induced-aggression

Appendix 7

Maximum BNF Doses for Adults and Elderly patients in 24hours

Drug	Route	Dose	Max. Dose /24hrs	Administration
Lorazepam	PO	2-4mg	4mg	Can be used sublingually
Lorazepam	IM	2-4mg	4mg or calculate using body weight; 30mcg/kg adult 15mcg/kg elderly	Must be diluted 1:1 with normal Saline or Water for Injection BP immediately before IM administration. **Flumazenil must be available**
Haloperidol	PO	5-10mg	20mg	A lower maximum dose would normally be used in the elderly
Haloperidol	IM	5-10mg	12mg (elderly - 6mg)	Bioavailability from the oral route is about 60% of that from the IM route, and readjustment of dose may be required.
Olanzapine	PO	10-15mg	20mg	The oral dispersible tablet should be placed on the tongue with plenty of water; it can be dissolved in water, coffee, milk, orange or apple juice.
Olanzapine	IM	10mg	20mg (3 injections)	Not to be given IV or subcutaneously.

Specialist advice

Aripiprazole	PO /IM	15-30mg (Initial dose 9.75mg for IM)	30mg	Available in IM injection, tablets, oral dispersible tablets and solution. Enhanced efficacy at oral daily doses higher than a 15mg has not been demonstrated.
Diazepam	IV	10mg	30mg	IM should never be used as very erratic and slow absorption. Diazemuls must be used IV. Give as slow IV injection (5mg / minute). Produces very rapid response. **Flumazenil must be available**
Levomepromazine	PO	25-50mg	1g	Highly sedative, no QTc prolongation data, but probably prolongs.
Levomepromazine	IM	25-50mg	200mg	Highly sedative, no QTc prolongation data, but probably prolongs.
Promethazine	PO	25mg	60mg	Can be used in patients who are benzodiazepine tolerant. Slow onset of action but highly sedating.
Promethazine	IM	25-50mg	100mg	Deep IM injection. Can be used in patients who are benzodiazepine tolerant. Slow onset of action but highly sedating.
Quetiapine	PO	50-100mg	800mg	Potentially highly sedative
Risperidone	PO	1-2mg	16mg	The oral dispersible tablet should be placed on the tongue with plenty of water.
Zuclopenthixol acetate (Acuphase®)	IM	50-150mg	See appendix 3	Not recommended for Rapid Tranquillization. (See appendix 3)

Appendix 8

Maximum Recommended Doses in 24hours for Children and Adolescents

Drug	Route	Dose	Max. Dose /24hrs	Administration
Lorazepam	PO	<12 years: 0.5-1mg >12 years: 1-2mg	4mg	Can be used sublingually
Lorazepam	IM	<12 years: 0.5-1mg >12 years: 1-2mg	4mg	Must be diluted 1:1 with normal Saline or Water for Injection BP immediately before IM administration. **Flumazenil must be available**
Olanzapine	PO	<12 years: N/A >12 years: 5mg	20mg	The oral dispersible tablet should be placed on the tongue with plenty of water; it can be dissolved in water, coffee, milk, orange or apple juice.
Olanzapine	IM	<12 years: N/A >12 years: 5-10mg	20mg (3 injections)	Not to be given IV or subcutaneously.
Promethazine	PO	<12 years: 5-10mg >12 years: 10-25mg	<12 years: 25mg >12 years: 50mg	Slow onset of action. Highly sedating.
Promethazine	IM	<12 years: 5-10mg >12 years: 10-25mg	<12 years: 25mg >12 years: 50mg	Deep IM injection. Slow onset of action. Highly sedating.

Specialist advice

Haloperidol	PO	<12 years: 0.5-1mg >12 years: 1-2mg	<12 years: 10mg >12 years: 15mg	+/- procyclidine.
Haloperidol	IM	<12 years: 0.5-1mg >12 years: 1-5mg	<12 years: 3mg >12 years: 12mg	Bioavailability from the oral route is about 60% of that from the IM route, and readjustment of dose may be required.
Risperidone	PO	0.5-2mg	<12 years: 2mg >12 years: 4mg	The oral dispersible tablet should be placed on the tongue with plenty of water.

Appendix 9

Pharmacokinetics

Drug	Route	Onset of Action*	Peak Concentration	Duration	Half Life
Aripiprazole	PO	NR	3-5 hrs	NR	75 hrs
Aripiprazole	IM	NR	1-3 hrs	NR	75hrs
Lorazepam**	PO	20-30mins	2 hrs	6-8 hrs	12 hrs
Lorazepam	IM	< 20-30mins	1-3 hrs	6-8 hrs	12 hrs
Haloperidol	PO	>1 hr	2-6 hrs	NR	21 hrs
Haloperidol	IM	20 mins	60-90 mins	NR	21 hrs
Olanzapine***	PO	1 hour	6 hrs	NR	21-54 hrs
Olanzapine	IM	15-30mins	15-45mins	NR	21-54 hrs
Diazepam	IV	NR	8mins	15-30mins	20-54 hrs
Levomepromazine	PO	NR	2-3 hrs	NR	30 hrs
Levomepromazine	IM	NR	30-120mins	NR	30hrs
Promethazine	PO	NR	2-3 hrs	4-6 hrs	7-15 hrs
Promethazine	IM	1-2 hrs	NR	4-6 hrs	7-15 hrs
Quetiapine	PO	NR	NR	NR	7 hrs
Risperidone***	PO	NR	1 hr	NR	20-30 hrs
Zuclopenthixol acetate (Acuphase®)	IM	1-8 hrs	24-48 hrs	48-72 hrs	20 hrs

NB: The above data correlates to use in adults. Evidence available suggests pharmacokinetics of the above are similar in child and adolescent population.

NR = Not reported
* Onset of sedation
** In some cases sublingual lorazepam may result in a faster onset of action than orally administered lorazepam. Sublingual administration of lorazepam also compares favorably in time to onset with intramuscular injection.
*** Velotabs and Quicklets have no buccal absorption; therefore their onset of action is the same as the non-dispersible tablet.

APPENDIX 10 – Drugs known to prolong QT Interval - as of 20th November 2008

This list includes drugs prescribed abroad, which patients may be admitted on. Advice can be obtained from pharmacy on the active ingredient in overseas products.

Disclaimer:

1. Concomitant administration of enzyme-inducing or -inhibiting drugs (e.g., anti-retrovirals, macrolide antibiotics), with drugs known to prolong the QT interval that are metabolised by these enzymes, may result in a potentiated QT interval prolongation.
2. Drugs with particular modes of action that involve electrolyte or fluid disturbances (e.g., diuretics) may affect blood potassium levels. Hypo- or hyper-kalaemia can induce cardiac arrhythmias, which may manifest as QT interval prolongation.
3. Certain drugs (e.g. cytotoxics) may cause cardiac toxicity. This may result in QT interval prolongation.

Cardiovascular drugs

Antiarrythmic drugs

Adenosine
Amiodarone
Bretylium
Disopyramide
Flecainide
Mexiletine (discontinued)
Procainamide
Propafenone
Quinidine
Sotalol

Vasodilator/anti-ischaemic drugs

Bepridil
Cilostazol (Pletal®)
Ivabradine (Procoralan®)
Lipoflazine
Papaverine
Prenylamine

Psychiatric drugs

Antidepressants

Amitriptyline
Amoxapine
Citalopram
Clomipramine
Desipramine
Dosulepin hydrochloride
Doxepin
Escitalopram
Imipramine
Lofepramine
Maprotiline
Moclobemide – at high dose
Nortriptyline
Paroxetine
Sertraline
Trazodone
Trimipramine
Venlafaxine

Conventional antipsychotics

Chlorpromazine
Flupenthixol (high doses)
Fluphenazine
Haloperidol
Mesoridazine
Pericyazine/periciazine
Perphenazine
Pimozide
Promazine
Sulpiride
Sultopride
Thioridazine
Trifluoperazine
Zuclopenthixol (higher doses)

Atypical antipsychotics

Amisulpride
Aripiprazole
Clozapine
Melperone (not licensed in UK)
Olanzapine
Paliperidone
Quetiapine
Risperidone
Sertindole
Ziprasidone
Zotepine

Other psychiatric drugs

Lithium
Chloral hydrate

Antihistamines

Astemizole
Diphenhydramine
Fexofenadine Hydrochloride – 1 case reported
Hydroxyzine
Mizolastine (Mizollen®)
Promethazine
Terfenadine

Antimicrobial and antimalarial drugs

Macrolide antibiotics
Azithromycin
Clarithromycin
Clindamycin – 1 case reported
Erythromycin
Telithromycin (Ketek®)

Fluoroquinolone antibiotics
Ciprofloxacin
Grepafloxacin
Levofloxacin
Moxifloxacin
Nalidixic acid
Ofloxacin
Sparfloxacin

Imidazole antifungals
Fluconazole
Itraconazole
Ketoconazole
Posaconazole
Voriconazole (Vfend®)

Antimalarials
Artemether with Lumefantrine (Riamet®)
Chloroquine
Halofantrine
Mefloquine (Lariam®)
Quinine

Other antimicrobials
Ampicillin
Co-Trimoxazole
Spiramycin
Pentamidine isetionate (Pentacarinat ®)
Quinuprisin and dafopristin (Synercid®)
Spiramycin

Antiemetics

Amsacrine
Dolasetron
Domperidone
Droperidol
Granisetron
Ondansetron
Palonosetron (Aloxi®)
Prochlorperazine
Tropisetron

Antineoplastics

Bicalutamide
Bortezomib (Velcade ®)
Dasatinib (Sprycel ®)
Lapatinib (Tyverb ®)
Nilotinib (Tasigna ®)
Sunitinib (Sutent ®)
Tamoxifen

Miscellaneous drugs

Alfuzosin
Amantadine
Apomorphine
Artemether
Atomoxetine
Bupidine
Bupropion
Ciclosporin
Cisapride
Cocaine
Didanosine – 1 case reported
Doxapram
Famotidine – 1 case reported
Formoterol
Foscarnet
Fosphenytoin
Galantamine – at high dose
Lofexidine
Iopamidol
Lanthanum
Lopinavir with ritonavir (Kaletra)
Methadone
Nicardipine
Octreotide
Oxytocin
Sibrutamine hydrochloride
Sodium stibogluconate
Solifenacin (Vesicare ®)
Sumatriptan
Tacrolimus
Tizanidine
Terodiline (discontinued in 1991 due to arrhythmias)
Tolterodine
Vardenafil
Vasopressin

Appendix 11 – Glossary of Terms

Advance directives (See Trust guidance on advance directives)

These are written instructions agreed between a patient and health professional before treatment begins, in which the patient specifies his or her preferred treatments and identifies the treatments he or she does not wish to receive. They guide health professionals in the event that the patient becomes unable to make decisions for him or herself.

Akathisia (restlessness)

A subjectively unpleasant state of inner restlessness where there is a strong desire or compulsion to move. Foot stamping when seated, constantly crossing/ uncrossing legs and/or constantly pacing up and down. Akathisia may be mistaken for psychotic agitation, leading to a cycle of increasing doses. It has also been linked with suicide and aggression towards others.

Disinhibition with benzodiazepines[3]

Disinhibition with benzodiazepines is an uncommon paradoxical reaction characterised by acute excitement and an altered mental state: increased anxiety, vivid dreams, hyperactivity, sexual disinhibition, hostility and rage. A history of aggression or impulsivity, neurological disorders, learning disability, age under 18 or over 65 are significant risk factors. Ingestion of alcohol can increase the severity of this reaction. The reaction is dose dependent with higher doses associated with a higher risk, particularly IV doses. Failure to recognise the reaction may result in the administration of higher doses of benzodiazepines thereby exacerbating the reaction. Antipsychotics drugs should be used to treat behavioural disturbances if disinhibition with benzodiazepines is suspected.

Dyskinesia

A group of involuntary movements that appear to be a fragmentation of the normal smoothly controlled limb and facial movements.

Dystonia

Muscle spasm in any part of the body e.g. eyes rolling upwards (oculogyric crisis) or head and neck twisted to the side (torticollis). The patient may be unable to swallow or speak clearly. In extreme cases the back may arch or the jaw dislocate.

Extrapyramidal side effects (EPSE)

Drug induced side effects especially caused by antipsychotics. These include dystonia, akathisia, pseudo-parkinsonism or dyskinesia. They can be acute or delayed.

Gillick Competence

Term used in medical law to decide whether a child (aged 16 years or younger) is able to consent to his or her own medical treatment, without the need for parental permission or knowledge.

Neuroleptic Malignant Syndrome (NMS)

NMS is a rare but potentially fatal dose-dependent adverse effect of all antipsychotics. The incidence is reported as being 0.07% to 0.15%, but the death rates have been reported at 14% and 38% for oral and depot medication respectively. The signs and symptoms are fever and severe muscle rigidity, sweating, incontinence, altered consciousness, confusion, tachycardia, altered blood pressure, altered LFTs, leucocytosis and raised creatinine kinase

Pseudo-parkinsonism

Tremor and or/rigidity, bradykinesia (decreased facial expression, flat monotone voice, slow body movements), bradyphrenia (slowed thinking) and salivation. Pseudoparkinsonism can be mistaken for depression or the negative symptoms of schizophrenia.

QTc prolongation

QTc is a measurement obtained from an ECG. If this is above normal limits (440ms for men and 470ms for women) it may predict a risk factor for the ventricular arrhythmia Torsade de Pointes, which is occasionally fatal (sudden cardiac death). Psychotropic agents have been associated with QTc prolongation, although there is controversy over the extent to which QTc prolongation is a risk factor. Above 500ms there is strong evidence for increased risk of arrhythmias. QTc prolongation may occur more frequently with high doses, intravenous administration and in predisposed patients. Check Maudsley guidelines [2] for risk of QTc prolongation.

Reduced respiratory rate

Rate of below 10 breaths per minute, can be caused by benzodiazepines.