BELMATT
HEALTHCARE TRAINING

Rapid Tranquilisation

Lecturer Details

Session Aims and Objectives

This session aims to:

- Highlight that rapid tranquilisation is an option of last resort
- Recognise the role of rapid tranquilisation in minimising risk to the patient or others
- Ensure no harm by establishing safe prescribing regimes and physical monitoring

The goal of rapid tranquillisation is “to achieve a state of calmness without sedation, sleep or unconsciousness, thereby reducing the risk to self and/or others while maintaining the ability of the patient to respond to communication”(NICE, 2005) when appropriate psychological and behavioural approaches have failed to de-escalate acutely disturbed behaviour.

A single as required dose of oral medication is not rapid tranquilisation.

Definition

- **Rapid Tranquilisation Definition**
- Rapid tranquilisation is the administration of lorazepam and/or an antipsychotic via the parenteral route, or repeated oral administration within 60 minutes.
- **A single dose of 'as required' oral medication is not considered rapid tranquilisation.**
- Rapid tranquilisation replaces the term emergency sedation

Patient Safety

The safety of the patient and others is the primary focus of. There are various considerations:

- **Non Pharmacological Approaches** – can these methods be used to improve the situation?
- **Cumulative Antipsychotic Dose** – Take into account regular prescriptions. If not,it is possible to exceed maximum daily dose of antipsychotics placing the patient at increased risk of adverse events
- **Combinations** – the use of two or more antipsychotics should be avoided where possible due to the risk of additive side effects including QT prolongation. This is a particularly important consideration in rapid tranquilisation where the patient's physical state predisposes to cardiac arrhythmia.
- **Age Specific Doses** – there are important differences in the medication and doses in older adults and young people compared to in adults aged 18-65. This is covered in the age-specific algorithms.
- **Co-morbid neurological disorders** – be aware of the risk of antipsychotics, especially in Parkinsons Disease and Lewy Body dementia where these medications should be avoided, and in epilepsy where the seizure threshold is reduced.

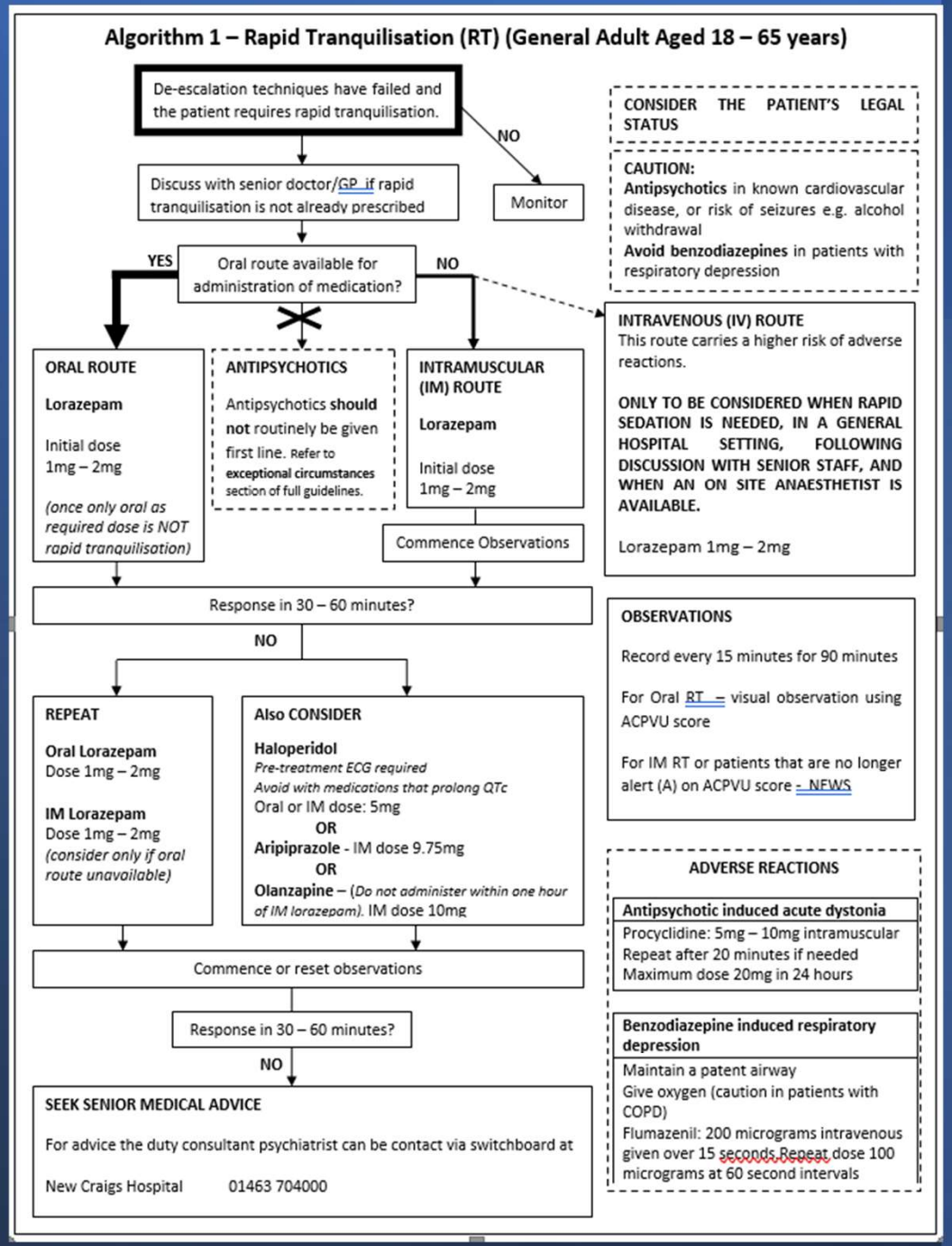
Key Guideline Updates

- A benzodiazepine (lorazepam) is the first line drug of choice to achieve rapid tranquilisation.
- Antipsychotic medication is considered a second line medication, but can be considered first line in exceptional circumstances.

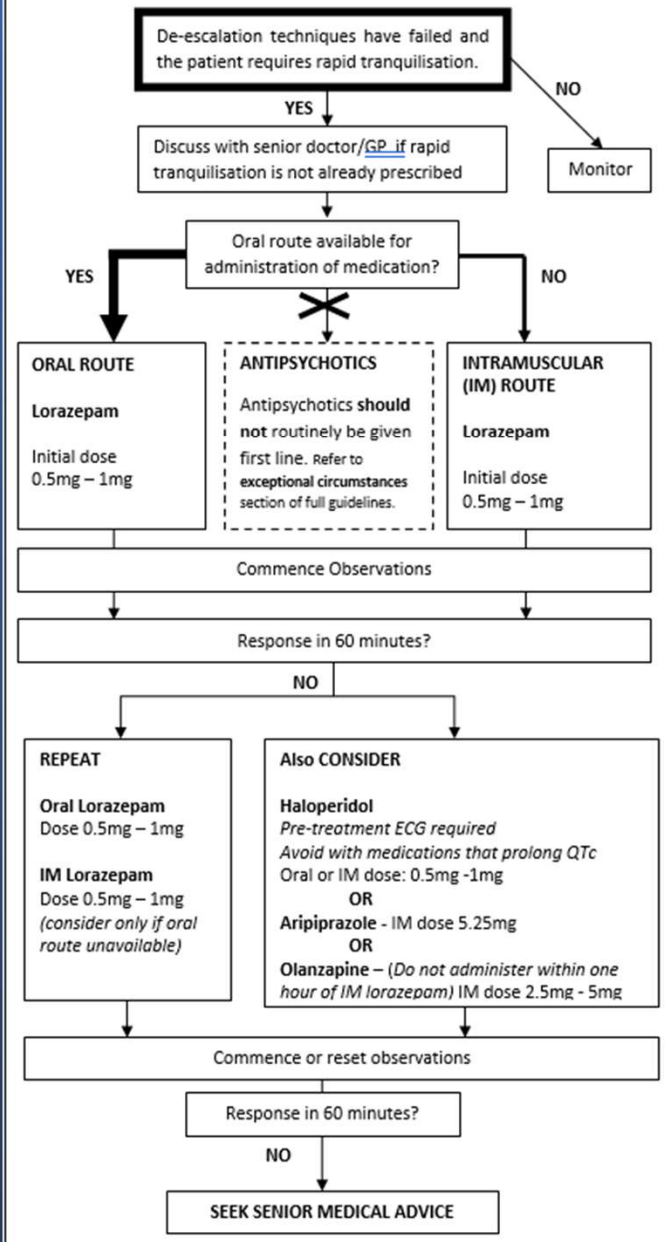
The use of haloperidol has the following important updates:

- Haloperidol can prolong the QTc and is contraindicated with other such medications (see Appendix 1 for a list of common medications that can prolong the QTc).
- The use of haloperidol in such a combination renders treatment unlicensed and should be avoided where possible. If clinical circumstances make the use of such combinations unavoidable and all other options have been considered ensure the rationale for treatment is clearly documented. Consider increased monitoring of ECG and biochemical parameters.
- The SPC for haloperidol requires a pre-treatment ECG. If circumstances make this impractical avoid haloperidol, or if use is unavoidable a clear justification must be documented.
- The maximum cumulative dose of haloperidol over 24 hours (oral and/or IM) in adults aged 18 years and above is now 20mg. The maximum cumulative dose in elderly patients is 5mg over 24 hours.

Algorithm 1 – Rapid Tranquilisation (RT) (General Adult Aged 18 – 65 years)



Algorithm 2 – Rapid Tranquilisation (RT) in older adults (typically over 65 years)



CONSIDER THE PATIENT'S LEGAL STATUS

CAUTION:

Antipsychotics should not be prescribed in Lewy Body Dementia or Parkinson's disease. Use cautiously in cardiovascular disease, or risk of seizures e.g. alcohol withdrawal

Benzodiazepines should be used with caution in patients with a diagnosis of delirium, respiratory depression or in those who have had previous paradoxical reactions.

OBSERVATIONS

Record every 15 minutes for 90 minutes

For oral RT – visual observation using ACPVU score

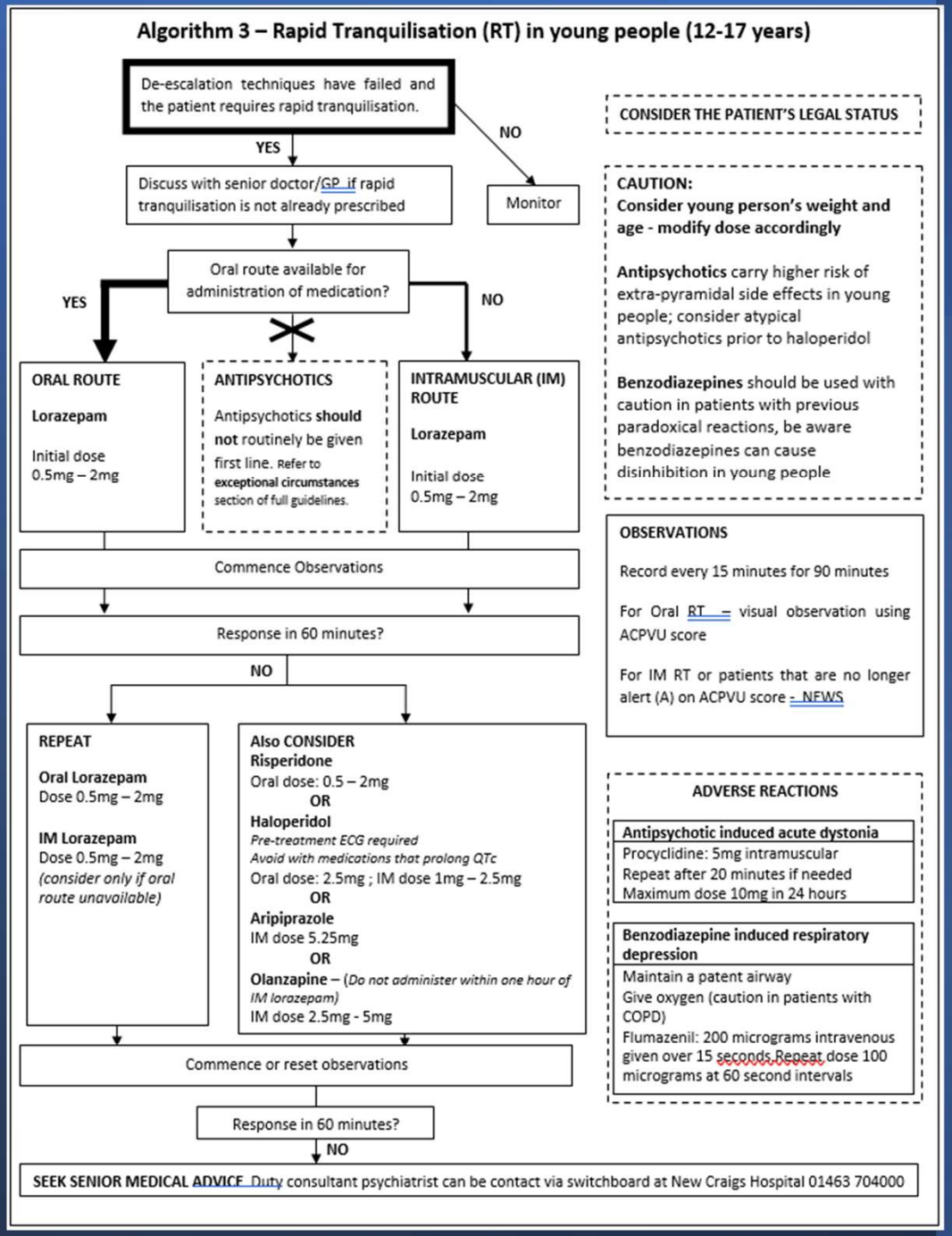
For IM RT or patients that are no longer alert (A) on ACPVU score – NEWS

ADVERSE REACTIONS

Antipsychotic induced acute dystonia
Procyclidine: 5mg intramuscular Repeat after 20 minutes if needed Maximum dose 10mg in 24 hours

Benzodiazepine induced respiratory depression
Maintain a patent airway Give oxygen (caution in patients with COPD) Flumazenil: 200 micrograms intravenous given over 15 seconds Repeat dose 100 micrograms at 60 second intervals

Algorithm 3 – Rapid Tranquilisation (RT) in young people (12-17 years)



Appendix 1: Physiological Risk Factors for QTc Prolongation and Arrhythmia

	Symptom/sign
Cardiac	•Long QT syndrome •Bradycardia •Ischaemic heart disease •Myocarditis •Myocardial infarction •Left ventricular hypertrophy
Metabolic	•Hypokalaemia •Hypomagnesaemia •Hypocalcaemia
Others	•Extreme physical exertion •Stress or shock •Anorexia nervosa •Extremes of age •Female gender

Drugs Associated with QT prolongation – this list is not exhaustive. Please refer to www.crediblemeds.org for more detailed information

Antipsychotic effect on QTc	
Effect	**Medication**
Nil	•Brexpiprazole •Cariprazine •Lurasidone
Low	•Aripiprazole •Asenapine •Clozapine •Flupentixol •Fluphenazine •Loxapine •Perphenazine •Prochlorperazine •Olanzapine •Paliperidone •Risperidone •Sulpiride
Moderate	•Amiulpride •Chlorpromazine •Haloperidol •Iloperidone •Levomepromazine •Melperone •Quetiapine •Ziprasidone
High	Any IV antipsychotic Pimozide Sertindole Any exceeding maximum dose
Unknown	•Pipotiazine •Trifluoperazine •Zuclopenthixol

Non-psychotropics associated with QTc prolongation	
Medication class	**Medication**
Antibiotics	•Erythromycin •Clarithromycin •Ampicillin •Co-trimoxazole •Pentamidine •(4 quinolones effect QTc – see manufacturers' literature)
Antimalarials	•Chloroquine •Mefloquine •Quinine
Antiarrhythmics	•Quinidine •Disopyramide •Procainamide •Sotalol •Amiodarone •Bretylium
Others	• Amantadine •Cyclosporin •Diphenhydramine •Hydroxyzine •Methadone •Nicardipine •Tamoxifen •Citalopram •Escitalopram

General Guidance

- Management plans for individual patients should be made in advance with a view to minimising the risk of acutely disturbed behaviour occurring.
- Consider non-pharmacological approaches
- Optimise regular medication
- If the patient requires oral “as required” psychotropic medication consider prescribing:
    - Benzodiazepines
    - Additional “as required” doses of the regular antipsychotic rather than introducing a second antipsychotic (being aware of the potential for this to trigger high dose antipsychotic therapy)
    - Promethazine
- Early intervention is desirable as disturbed behaviour should be brought under control as soon as possible.
- Initial attempts should be made to use a non-pharmacological approach rather than medication.
- Consider and address physical causes for behaviour.

Non Pharmacological Approaches

- Whilst medication will continue to have a significant role to play in keeping the situation safe, non pharmacological approaches can significantly reduce the need for such medication. De-escalation techniques can be used where the situation is likely to involve anger, irritation, aggression or risk of violence. In such situations it is incumbent upon the service to provide staff training in de-escalation that enables them to:
- Recognise the early signs of agitation, irritation, anger and aggression.
- Understand the likely causes of aggression or violence, both generally and for each service user.
- Use techniques for distraction and calming, and ways to encourage relaxation.
- Recognise the importance of personal space.
- Respond to a service user's anger in an appropriate, measured and reasonable way and avoid provocation.
- Re-enforce pre-existing de-escalation and emotional regulation skills.

Rapid Tranquilisation Medications

Route

- The oral route should always be considered first and used if at all possible.
  If oral medication is not possible then consider the intramuscular (IM) route.
  The intravenous (IV) route should only be considered in very rare circumstances. Please refer to 'general hospital setting' for details.

Choice

- A benzodiazepine (lorazepam) is the first line drug of choice to achieve rapid tranquilisation.
- Antipsychotic medication is considered a second line medication, but can be considered first line in exceptional circumstances (see section on exceptional circumstances).
- Avoid lorazepam in patients with compromised respiratory function.
- Caution using lorazepam in combination with clozapine (respiratory depression in rare cases).
- Assess risk factors for QTc prolongation and avoid antipsychotics in patients with compromised cardiovascular function.
- The prescribing of rapid tranquilisation should take into account the patient's past response to medication, and any available advance statements.
- If there is a risk of seizures (such as known epilepsy or alcohol withdrawal) use a benzodiazepine rather than an antipsychotic as the latter can lower the seizure threshold.

Updates on use of haloperidol

- Haloperidol can prolong the QTc and is contraindicated with other such medications (see 'QTc Cautions and Contraindications' for a list of common medications that can prolong the QTc).
- The use of haloperidol in such a combination renders treatment unlicensed and should be avoided where possible. If clinical circumstances make the use of such combinations unavoidable and all other options have been considered ensure the rationale for treatment is clearly documented. Consider increased monitoring of ECG and biochemical parameters.
- The SPC for haloperidol requires a pre-treatment ECG. If circumstances make this impractical avoid haloperidol, or if use is unavoidable a clear justification must be documented.

- IM aripiprazole or IM olanzapine (unlicensed in UK) are potential alternative antipsychotics that may be preferable to IM haloperidol, depending on individual clinical circumstances. A decision to use these alternatives should be made by a senior doctor.
- IM olanzapine and an IM benzodiazepine must not be administered within 1 hour of each other.

Important Considerations

- **Safety**
- **Avoid**
- Do not mix lorazepam and an antipsychotic in the same syringe.
- **Ensure**
- Flumazenil is readily available.
- Oral and IM procyclidine is readily available.

Use of Flumazenil

Flumazenil is used to reverse the respiratory depression caused by benzodiazepines. It is anticipated that IM administration of benzodiazepines is unlikely to produce this effect. However the use of IM midazolam does increase this risk due to potential drug interactions involving midazolam but not lorazepam.

If required, flumazenil should be given by IV injection, 200 micrograms over 15 seconds, then 100 micrograms at 60 second intervals if required. Flumazenil has a short half-life and therefore subsequent doses may be necessary. Usual dose range 300 to 600 micrograms. Maximum total dose = 1mg in 24 hours (one initial dose and eight subsequent doses).

ECG

- It is usually impractical to obtain an ECG from a patient who requires rapid tranquilisation.
- ECG as soon as it is practical
- High risk of ventricular arrythmias
- Any medication which can prolong the QT interval should be stopped if the ECG shows a QTc of greater than 500ms.

Midazolam (alternative to Lorazepam Injection when unavailable)

- Midazolam injection is the recommended alternative to lorazepam injection
- Speed of onset of sedation with midazolam is around 15 minutes, which is two to three times more rapid than lorazepam.
- Midazolam can interact with other medication

Clopixol Acuphase

- Clopixol Acuphase (zuclopenthixol acetate) is not recommended for rapid tranquilisation due to a long onset and duration of action. If considering its use please refer to 'exceptional circumstances'.

Antipsychotics in Rapid Tanquilisation and the High Dose Protocol

- Care should be taken to avoid combinations and high cumulative doses of antipsychotics where possible.

Antipsychotics could be considered in the following circumstances:

- Where benzodiazepine prescription alone has been unsuccessful or contraindicated
- In patients with a known positive response to antipsychotic medication
- Where the patient indicates they would prefer antipsychotic medication (e.g. advanced statement).
- In a patient with delirium

Before prescribing an antipsychotic, carefully consider the following:-

- Is the patient antipsychotic-naïve?
- Is there a risk of seizures (e.g. known epilepsy, alcohol withdrawal).
- Does the patient have a history of adverse reactions to antipsychotics?
- Are there any cardiac co-morbidities?
- Is the patient currently prescribed other antipsychotic medication?
- Does the patient have a co-morbid neurological disorder? - especially Parkinson's disease or Lewy body dementia where antipsychotics should be avoided.

- When an antipsychotic is prescribed, it is important to consider the total amount of different antipsychotic prescribed.

Prescribing of Rapid Tranquilisation

- **Refer to** Rapid Tranquilisation Algorithms as a guide when prescribing. See your local policy.
- On admission the decision to prescribe rapid tranquilisation should be recorded in the Assessment/Admission booklet. Otherwise clearly document the reasons in the patient's notes.
- The review of this decision should be at the initial senior review, and at each ward round.

Review within 24 for :

- Alteration to the patient's regular treatment.
- Alteration to the prescribing of as required or rapid tranquilisation as a result of the patient's response to the medication administered.

Prescribing Information

- **Lorazepam**
- Dose (oral, IM or IV) in patients aged 18-65 is 1mg to 2mg.
- The bioavailability of the oral and intramuscular routes are similar.
- The speed of onset of sedation is similar for both routes.
- The maximum cumulative dose (oral and/or IM) is 8mg in 24 hours.
- Also take into consideration any other benzodiazepines that the patient is prescribed

Older Adults Population Over 65yrs

General principles

- Over sedation or unconsciousness is particularly dangerous in frail adults and should not be considered a successful outcome.
- Consider and address physical causes for behaviour.
- Older adults may respond to lower doses and may take longer to respond.
- Start with the lowest appropriate dose and titrate slowly upwards if necessary.
- If the oral route (preferable) is unavailable use intramuscular (IM) route with caution.

Avoid the intravenous (IV) route.

- Patients with renal or hepatic insufficiency may require a lower initial dose, with subsequent adjustments at smaller increments and at longer intervals.
- Consider the risk of falls when using sedative medication in this population.
- Avoid procyclidine use where possible.
- **If in doubt seek advice from psychiatry.**

Prescribing Information

- A benzodiazepine (lorazepam) is the drug of choice to achieve rapid tranquilisation.
  Antipsychotic medication can be considered an alternative in exceptional circumstances (see main policy section and algorithm for older adults)

Lorazepam

- Benzodiazepines are best avoided if delirium is diagnosed or suspected.
- Lorazepam is contra-indicated in patients with respiratory depression or severe hepatic insufficiency.
- Paradoxical reactions to benzodiazepines occur in less than 1% of patients however older adults may be more predisposed to these reactions.

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•Lorazepam is contra-indicated in patients with respiratory depression or severe hepatic insufficiency.

•Paradoxical reactions to benzodiazepines occur in less than 1% of patients however older adults may be more predisposed to these reactions.

•The bioavailability and speed of onset of sedation is similar for both oral and IM routes

Haloperidol

•Haloperidol is contra-indicated in the lewy body dementias and Parkinson's disease.

•As highlighted in the '**General principles**' section of the guideline, there are specific considerations with haloperidol, QTc prolongation, and ECG monitoring.

•Avoid use in patients with compromised cardiovascular function or at risk of seizure.

•The IM route generally has significantly greater bioavailabilty than the oral route.

•The speed of onset of action between the oral and IM route is different.

**doses above 2.5 mg daily should only be considered in patients who have tolerated higher doses and after reassessment of the individual benefit-risk.

Alternative IM antipsychotics

If the use of haloperidol is inappropriate or contra-indicated, and IM antipsychotic medication is considered necessary, then aripiprazole or olanzapine can be considered as alternatives.

Aripiprazole

A repeat dose if needed can be administered after a minimum of two hours and up to three injections per 24 hour period.

Olanzapine

IM olanzapine as a short acting injection should not be administered within an hour of administering an IM benzodiazepine, especially if alcohol has been consumed.

A repeat dose if needed can be administered after a minimum of two hours; up to three injections per 24 hour period.

Algorithm 2

Haloperidol	Initial dose	Maximum Older Adult Dose**	Speed of onset of sedation	Duration of sedation	Time to peak
Oral	0.5mg to 1mg	2.5mg in 24 hours	1 to 2 hours	4 to 8 hours	2 to 6 hours
IM	0.5mg to 1mg	2.5mg in 24 hours	20 to 40 minutes	4 to 8 hours	20 to 40 minu

- **Haloperidol**
- Haloperidol is contra-indicated in the lewy body dementias and Parkinson's disease.
- As highlighted in the '**General principles**' section of the guideline, there are specific considerations with haloperidol, QTc prolongation, and ECG monitoring.
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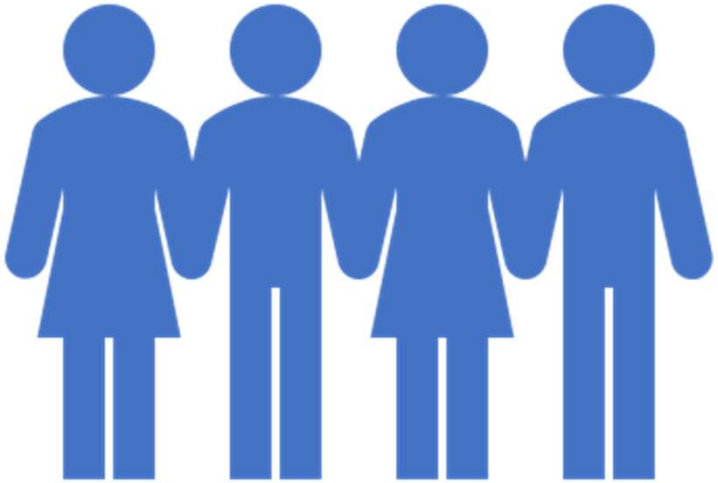


Young People

- Use intramuscular lorazepam for rapid tranquillisation in a child or young person and adjust the dose according to their age and weight.

  In May 2015, lorazepam was off label in children and young people for this indication.
- If there is only a partial response to intramuscular lorazepam, check the dose again according to the child or young person's age and weight and consider a further dose.
- Monitor physical health and emotional impact continuously when undertaking rapid tranquillisation in a child or young person.

Rapid Tranquilisation in Young People

- Ensure physical causes for acute behavioural disturbance are assessed and treated as appropriate – consider the impact of any physical co-morbidities, developmental disorders and substance use on presentation.
- Consider the young person's age and weight when prescribing – in general lower doses will be required in those < 40kg and / or < 16 years of age.
- Start with the lowest appropriate dose and titrate slowly upwards if necessary.
- If the oral route (preferable) is unavailable use intramuscular (IM) route with caution.
- **Avoid the intravenous (IV) route where possible.**
- **If able discuss use of rapid tranquilisation with Child and Adolescent Psychiatrist prior to use.**

The Administration of Rapid Tranquilisation

- Nursing staff may use their professional judgement to administer lorazepam and/or antipsychotic for rapid tranquilisation when this is prescribed. This decision requires two registered nurses

Lorazepam
Calculate the total amount of lorazepam that has been administered to the patient in the last 24 hours on all areas of the Kardex. This includes the “as required”, “once only”, regular prescription and rapid tranquilisation supplementary sheet. Ensure that the total dose administered in 24 hours from all routes does not exceed the maximum dose stated in the rapid tranquilisation prescription. If maximum cumulative dose has been reached you cannot administer any more lorazepam and would need a medical review.

Antipsychotic
Decision made by a senior doctor/GP

Dose should be clearly prescribed.

Recording What Has Been Administered via Rapid Tranquilisation and Follow-up

- For the administration of rapid tranquilisation, two nurses’ initials should be recorded on the kardex along with the dose administered
- All entries for rapid tranquilisation should be recorded in red pen
- Any incident requiring rapid tranquilisation and the effect of rapid tranquilisation should be recorded in the case notes
- Contact the patient’s consultant/duty consultant requesting that the patient be reviewed within 24 hours of administration of the rapid tranquilisation medication. See section on 'The Prescribing of Rapid Tranquilisation.'
- A post incident review should take place as soon as possible after the administration of rapid tranquilisation if restraint has been required.

Exceptional Circumstances

Clopixol Acuphase

- Clopixol Acuphase (zuclopenthixol acetate) is not recommended for rapid tranquilisation due to a long onset and duration of action, but may be considered as an option when:
- The patient is liable to be disturbed over an extended time period.
- There is a past history of good/timely response.
- There is a past history of repeated parenteral administration.
- Cited in an advance statement.
- The use of Clopixol Acuphase should be a consultant decision.
  Never administer to patients who are neuroleptic naïve.

Observation and Monitoring

- ACVPU score, to highlight if the patient is **A**lert, **C**onfused, responding to **V**oice or **P**ain, or **U**nresponsive.
- Blood pressure/pulse/respiratory rate every 5 minutes, temperature every 30 minutes and look for evidence of dystonia.
- Transfer (accompanied by staff) only when the patient has been stable for at least 30 minutes (calm and cardiovascular and respiratory observations stable).
- **heck the patient every 15 minutes for 90 minutes following the administration of rapid tranquilisation. This period can be extended if there are concerns, and restarted if further rapid tranquilisation is administered**

Monitoring

Problem/Change to Baseline	Remedial Action
Respiratory rate reduction to <10 breaths/minute or Oxygen Saturation <94% on pulse oximeter	Maintain a patent airway Give oxygen (caution in patients with COPD) Give IV flumazenil if benzodiazepine induced respiratory depression. If induced by any other sedative agent may require mechanical ventilation and transfer to medical care.
Increased temperature	Withhold antipsychotics if above 38^{o}C (risk of neuroleptic malignant syndrome and arrhythmia). Check creatinine kinase urgently.
Pulse increased >100 beats per minutes	Refer to medical care
Pulse decreased <60 beats per minutes	Refer to medical care
Fall in blood pressure of >20mmHg orthostatic drop, or systolic blood pressure <90mmHg, or diastolic blood pressure <50mmHg	Lie patient flat. Tilt bed towards head. Monitor closely.
Acute dystonia (including oculogyric crisis)	Give procyclidine 5mg to 10mg IM. Repeat after 20 minutes if necessary to maximum of 20mg/24 hours.

Monitoring inpatient

- Staff in inpatient psychiatric wards (including general adult wards, older adult wards, psychiatric intensive care units and forensic wards) should use the following definitions for levels of observation, unless a locally agreed policy states otherwise.
- Low-level intermittent observation: the baseline level of observation in a specified psychiatric setting. The frequency of observation is once every 30 to 60 minutes.
- High-level intermittent observation: usually used if a service user is at risk of becoming violent or aggressive but does not represent an immediate risk. The frequency of observation is once every 15 to 30 minutes.
- Continuous observation: usually used when a service user presents an immediate threat and needs to be kept within eyesight or at arm's length of a designated one-to-one nurse, with immediate access to other members of staff if needed.
- Multiprofessional continuous observation: usually used when a service user is at the highest risk of harming themselves or others and needs to be kept within eyesight of 2 or 3 staff members and at arm's length of at least 1 staff member.

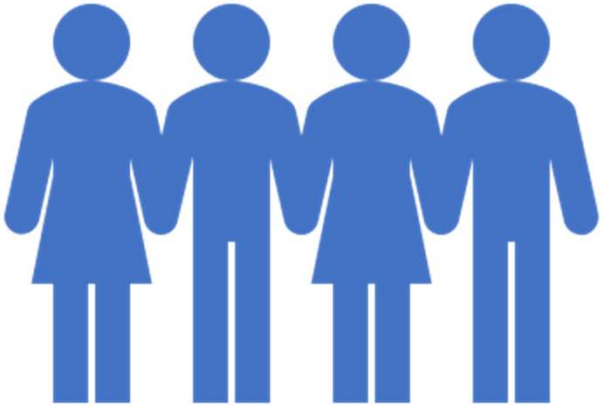
Documentation

- **Reasons for using RT**
- Legal situation (ie which part of the Mental Health Act used).
- Physical assessment - any medical hazards recognised.
- Patient's diagnosis.
- Drugs given - in what sequence and dosage.
- Outcome.
- Monitoring chart and ongoing plan.

Debrief

- Discuss, as a significant event, whether the need for RT could have been anticipated and prevented. Discuss the patient's account if available.

Prevention



- The establishment of verbal contact.
- Avoiding being provocative.
- Being concise.
- Listening closely to the patient
- Respecting the patient and their personal space.
- Negotiating and trying to agree or agreeing to disagree.
- Offering choices and optimism.
- Setting clear limits.
- Identifying the wants or feelings of the patient.
- Debriefing the patient and staff.
- Proactive de-escalation planning.

Care planning

- Do patients who might be subject to RT have an individual plan?
- Is this reviewed at least weekly?
- If RT is used, does a senior doctor review all medicines at least daily?
- **Does the plan record:**

❖ the target symptoms,

❖ the total daily dose of medication prescribed and administered, including prn,

❖the number and reason for any missed doses

❖ therapeutic response and the emergence of unwanted effects

❖ any advance decision by the patient about their treatment?

References

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