SECTION 8: MANAGEMENT OF ACUTELY DISTURBED BEHAVIOUR

Formulary and Prescribing Guidelines
### 8.1 Management of acutely disturbed ADULTS

(See CG52 for full guidelines)

- Before considering pharmacological measures:
  - Consider de-escalation, using non drug approaches: seclusion/moving to a low stimulus area, talking down, time out, distraction
  - If possible, do a mental state examination and physical state examination, take a history including drug/alcohol status, drug sensitivities, concurrent medication
  - Check for intercurrent illness and recent illicit substance use
  - Establish a working diagnosis
  - Check for any advance directive in relation to medicines

#### NON-PHARMACOLOGICAL MEASURES UNSUCCESSFUL OR INAPPROPRIATE

**LEVEL 1**

**Disturbed BUT accepting oral medication**

- nurse in a quiet area
- ongoing verbal de-escalation
- food and fluid to be provided
- review current medication
- decide whether additional medication required

**ORAL interventions (PO)**

- **Lorazepam (1-2mg; max 4mg in 24 hours)**
  - Can be repeated after 1 hour
  - OR
- **Promethazine (50mg; max 100mg /24 Hours)**
  - Can be repeated after 1 Hour
  - OR
- **Haloperidol (5-10mg; max 20mg po / 24 hours)**
  - Can be repeated after 1 hour
  - Ensure cardiac status of patient is known, preferably with previous ECG
  - OR
- **Risperidone (2mg)**
  - Orodispersible tablets may be considered if the patient is likely to spit out the tablets
  - Can be repeated after 2 hours
  - OR
- **Olanzapine (10mg)**
  - Orodispersible tablets may be considered if the patient is likely to spit out the tablet
  - Can be repeated after 2 hours

**LEVEL 2**

**Disturbed AND refusing oral medication**

- Review all medication prescribed within last 24 hours (BNF limits, side effects etc)
- Consultant opinion may have to be sought

**PARENTERAL interventions (IM)**

- **Lorazepam IM (1-2mg; max 4mg in 24 hours)**
  - Sedation in 30-45 minutes; peaks 1-3 hours; Lasts 4-6 hours
  - OR/AND
- **Promethazine IM (50mg)** (can repeated in 1-2 hours, if needed, up to max: 100 mg/day) may be used in benzodiazepine-tolerate patients and is the first line alternative during shortages of lorazepam
  - AND/OR
- **Haloperidol IM (5mg; max 12mg IM in 24 hours)**
  - Used as monotherapy or in combination with Lorazepam or Promethazine
  - Sedation in 10 minutes; peaks in 15-60 minutes; Half life 10-36 hours
  - Ensure cardiac status of patient is known, preferably with previous ECG
  - OR
- **Olanzapine IM as monotherapy (5-10mg; max 3 injections in 24 hours & Max 20mg in 24 Hours)**
  - Peaks in 15-45 minutes.
  - Do not repeat within 2 hours
  - Do not use Lorazepam IM within one hour of administering Olanzapine IM
  - OR
- **Aripiprazole IM (5.25mg-15mg:max 3 injections in 24hours). Max 30mg in 24 hours. Peaks in 1-3 hours**

**LEVEL 3**

- Consultant’s direct involvement mandatory
- Consult on-call pharmacist
- Second opinion of another consultant
- Avoid Diazepam if ECT is being considered

**Diazepam 10mg IV over at least 5 minutes.** Can be repeated up to 3 times if insufficient effect.
8.2 Management of acutely disturbed OLDER ADULTS

**Before considering pharmacological measures:** (see CG52 for more information)
- Consider de-escalation, using non drug approaches: seclusion/moving to a low stimulus area, talking down, time out, distraction
- If possible, do a mental state examination and physical state examination, taking into account frailty, drug/alcohol status, drug sensitivities, concurrent medication, dementia
- Check for intercurrent illness and recent illicit substance use
- Establish a working diagnosis
- Check for any advance directive in relation to medicines

**NON-PHARMACOLOGICAL MEASURES UNSUCCESSFUL OR INAPPROPRIATE**

**LEVEL 1**
Disturbed **BUT** accepting oral
- nurse in a quiet area
- ongoing verbal de-escalation
- food and fluid to be provided
- review current medication
- decide whether additional medication required

**ORAL interventions (PO)**
- **Lorazepam** (0.5-1mg; max 2mg/24H)
  - Can be repeated after 1 hour
  - Worsens confusion in BPSD
  - OR
- **Haloperidol** (0.75-1.5mg; max 5mg/24H)
  - Can be repeated after 1 hour
  - Ensure cardiac status of patient is known, preferably with previous ECG
  - OR
- **Risperidone** (0.5-1mg)
  - Orodispersible tablets may be considered if the patient is likely to spit out the tablets
  - Can be repeated after 2 hours
  - Preferred option in BPSD
  - OR
- **Olanzapine** (2.5-5mg)
  - Orodispersible tablets may be considered if the patient is likely to spit out the tablet
  - Can be repeated after 2 hours

**LEVEL 2**
Disturbed **AND** refusing oral medication
- Review all medication prescribed within last 24 hours (BNF limits, side effects etc)
- Consultant opinion may have to be sought

**PARENTERAL interventions (IM)**
- **Lorazepam IM** (0.5 -1mg; max 2mg/24H)
  - Sedation in 30-45 mins; peaks 1-3 hours; Lasts 4-6 hours,
  - Do not use lorazepam within one hour of administering olanzapine IM
  - OR
- **Promethazine IM** (25mg; 50mg/24H)
  - Can be repeated in 1-2 hours, may be used in benzodiazepine-tolerant patients
  - Promethazine is the first line alternative during shortages of lorazepam
  - OR
- **Haloperidol IM** (1-2.5mg; max 5mg/24H)
  - Use alone or in combination with lorazepam, sedation in 10 mins, peaks in 15-60 mins, half life 10-36 hours,
  - Ensure cardiac status of patient is known (ECG)
  - OR
- **Olanzapine IM as monotherapy** (5-10mg; max 20mg/24H)
  - Peaks in 15-45 mins
  - Do not repeat within 2 hours
  - OR
- **Aripiprazole IM** (5.25mg-15mg; max 3 injections in 24hours). Max 30mg in 24 hours. Peaks in 1-3 hours

**LEVEL 3**
- Refer to consultant
- Refer to consultant

Approved by Medicines Management Group February 2019
### 8.3 Management of acutely disturbed CHILDREN & ADOLESCENTS

**Before considering pharmacological measures:**  
(see CG52 for more information)
- Consider de-escalation, using non drug approaches: seclusion/moving to a low stimulus area, talking down, time out, distraction
- If possible, do a mental state examination and physical state examination, take a history including drug/alcohol status, drug sensitivities, concurrent medication
- Check for intercurrent illness and recent illicit substance use
- Establish a working diagnosis
- Check for any advance directive in relation to medicines

### NON-PHARMACOLOGICAL MEASURES UNSUCCESSFUL OR INAPPROPRIATE

**LEVEL 1**  
**Disturbed BUT accepting oral medication**
- nurse in a quiet area
- ongoing verbal de-escalation
- food and fluid to be provided
- review current medication
- decide whether additional medication required

If patient is unknown to services initially treat with Lorazepam and avoid antipsychotics if possible

<table>
<thead>
<tr>
<th><strong>ORAL interventions (PO)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam (over 12 years 1-2mg; max 4mg in 24 hours / Under 12 years 0.5-1mg; max 2mg in 24 hours) Can be repeated after 1 hour OR</td>
</tr>
<tr>
<td>Promethazine (over 10 years 25-50mg / between 5-9 years 20-25mg) Can be repeated after 1 hour OR</td>
</tr>
<tr>
<td>Risperidone (0.5-1mg) Orodispersible tablets may be considered if the patient is likely to spit out the tablets Can be repeated after 2 hours OR</td>
</tr>
<tr>
<td>Olanzapine (5mg) Orodispersible tablets may be considered if the patient is likely to spit out the tablet Can be repeated after 2 hours OR</td>
</tr>
<tr>
<td>Quetiapine (over 12 years 25-50mg / under 12 years 12.5-25mg) Can be repeated after 2 hours</td>
</tr>
</tbody>
</table>

**LEVEL 2**  
**Disturbed AND refusing oral medication**
- Review all medication prescribed within last 24 hours (BNF limits, side effects etc)
- Consultant opinion may have to be sought

<table>
<thead>
<tr>
<th><strong>PARENTERAL interventions (IM)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam IM (over 12 years 1-2mg; max 4mg in 24 hours / Under 12 years 0.5-1mg; max 2mg in 24 hours) Sedation in 30-45 minutes; peaks 1-3 hours; Lasts 4-6 hours OR</td>
</tr>
<tr>
<td>Promethazine IM (over 10 years 25-50mg / between 5-9 years 10-25mg) Promethazine is the first line alternative during shortages of lorazepam OR</td>
</tr>
<tr>
<td>Aripiprazole IM (5.25mg-15mg:max 3 injections in 24hours). Max 30mg in 24 hours. Peaks in 1-3 hours OR</td>
</tr>
<tr>
<td>Olanzapine IM as monotherapy (over 12 years 5-10mg: max 3 injections/20mg in 24 hours) Peaks in 15-45 minutes. Do not repeat within 2 hours Do not use lorazepam within one hour of administering olanzapine IM</td>
</tr>
</tbody>
</table>

Approved by Medicines Management Group February 2019
### 8.4 Drugs approved for management of acute disturbed behaviour

See latest BNF for licensed indications.

<table>
<thead>
<tr>
<th>Drug and form</th>
<th>Time to max. plasma Conc.</th>
<th>Half life</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol IM injection</td>
<td>15-60 mins</td>
<td>10-36 hours</td>
<td>The maximum daily dose shown above for adults (12mg) does not match that shown in the current BNF (20mg) and SPC (20mg – this dose updated September 2017). The lower dose of 12mg is based on that published in older BNFs and SPCs, and recent consensus guidelines from BAP/NAPICU (2018), which state: the IM dose required to give the same plasma concentration as any given oral dose is approximately 30% lower (due to the difference in the magnitude of first pass liver metabolism). A 12mg adult maximum for IM is used by several other MH&amp;LD Trusts in the UK.</td>
</tr>
<tr>
<td>Haloperidol solution</td>
<td>3-6 hours</td>
<td>10-36 hours</td>
<td></td>
</tr>
<tr>
<td>Haloperidol tab</td>
<td>3-6 hours</td>
<td>10-36 hours</td>
<td></td>
</tr>
<tr>
<td>Lorazepam IM injection</td>
<td>60-90 mins</td>
<td>12-16 hours</td>
<td>Lorazepam should be used with caution in elderly due to the risk of sedation and/or musculoskeletal weakness that can increase risk of falls, with serious consequences. These patients should be given a reduced dose (50%) and titrated accordingly. The FDA has warned of a serious risk of death when benzodiazepines are used in combination with opioid analgesic or cough preparations.</td>
</tr>
<tr>
<td>Lorazepam tabs</td>
<td>2 hours</td>
<td>12 hours</td>
<td></td>
</tr>
<tr>
<td>Olanzapine dispersible tab.</td>
<td>5-8 hours</td>
<td>32-50 hours</td>
<td>IM olanzapine may produce a 5-fold increase in plasma conc. vs. the same dose given orally</td>
</tr>
<tr>
<td>Olanzapine injection</td>
<td>15-45 mins</td>
<td>32-50 hours</td>
<td></td>
</tr>
<tr>
<td>Olanzapine tab</td>
<td>5-8 hours</td>
<td>32-50 hours</td>
<td></td>
</tr>
<tr>
<td>Promethazine IM injection</td>
<td>2-3 hours</td>
<td>5-14 hours</td>
<td></td>
</tr>
<tr>
<td>Risperidone dispersible tab.</td>
<td>1-2 hours</td>
<td>24 hours</td>
<td></td>
</tr>
<tr>
<td>Risperidone liquid</td>
<td>1-2 hours</td>
<td>24 hours</td>
<td></td>
</tr>
<tr>
<td>Risperidone tab</td>
<td>1-2 hours</td>
<td>24 hours</td>
<td></td>
</tr>
</tbody>
</table>

Clonazepam IM is non-formulary due to the fact that it is an unlicensed preparation in the UK. It is an intravenous product and IM use is an “Off label” indication. If clonazepam is required it should be requested on a “non-formulary form” and there should be an entry in the patient’s healthcare record that a full discussion has taken place with the patient and that they have given informed consent for it to be prescribed.

### 8.5 Guidelines for the use of Flumazenil
Flumazenil is a specific reversal agent for benzodiazepine-induced respiratory depression. It is held at all sites where injectable lorazepam is stocked.

<table>
<thead>
<tr>
<th>Indications for use</th>
<th>If the respiratory rate falls below 10/minute after the administration of lorazepam (diazepam or midazolam)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contra-indications</td>
<td>Patients with epilepsy who have been receiving long-term benzodiazepines</td>
</tr>
<tr>
<td>Caution</td>
<td>Dose should be carefully titrated in hepatic impairment</td>
</tr>
<tr>
<td>Dose and route of administration</td>
<td>Initially 200 mcg intravenously* over 15 seconds (10 mcg/kg max single dose 200 mcg in children under 12 years)</td>
</tr>
<tr>
<td></td>
<td>If the required level of consciousness is not achieved after 60 seconds then subsequent dose: 100 mcg intravenously over 10 seconds</td>
</tr>
<tr>
<td></td>
<td>* IV injection of flumazenil must be given by a doctor.</td>
</tr>
<tr>
<td>Time before dose can be repeated</td>
<td>60 seconds</td>
</tr>
<tr>
<td></td>
<td>Further doses of 100 mcg can be repeated at 60 second intervals where necessary to a maximum of 1 mg</td>
</tr>
<tr>
<td>Maximum dose</td>
<td>1 mg in 24 hours (one initial dose and eight subsequent doses)</td>
</tr>
<tr>
<td>Side effects</td>
<td>Patients may become agitated, anxious or fearful on awakening</td>
</tr>
<tr>
<td></td>
<td>Seizures may occur in regular benzodiazepine users</td>
</tr>
<tr>
<td>Management</td>
<td>Side effects usually subside</td>
</tr>
<tr>
<td>Monitoring</td>
<td>• What to monitor?</td>
</tr>
<tr>
<td></td>
<td>Respiratory rate</td>
</tr>
<tr>
<td></td>
<td>• How often?</td>
</tr>
<tr>
<td></td>
<td>Continuously until respiratory rate returns to baseline level. Flumazenil has a very short half life so respiratory function may appear to recover and then deteriorate again.</td>
</tr>
<tr>
<td></td>
<td>Note: if respiratory rate does not return to normal or patient is not alert after initial doses given then assume sedation due to some other cause.</td>
</tr>
</tbody>
</table>

### 8.6 Acute Disturbed Behaviour Monitoring

Monitoring of vital signs must be recorded using the MEWS Form or Track and Trigger and filed in the patient’s healthcare record. This should also be used to record situations where it is not possible to monitor vital signs along with the reason why.

After any parenteral drug administration, monitor and record on the MEWS chart the following:

1. Temperature  
2. Pulse  
3. Blood pressure  
4. Respiration rate

Every 5-10 minutes for one hour and then half hourly until patient is ambulatory. If the patient is asleep or unconscious, the continuous use of pulse oximetry to measure oxygen saturation is desirable. A nurse should remain with the patient until ambulatory. ECG and haematological monitoring are also necessary when parenteral antipsychotics are administered, especially when higher doses are used. Hypokalaemia, stress and agitation
place the patient at risk of cardiac arrhythmias. A crash bag should be available within 3 minutes.

### 8.7 Remedial Measures in ADULTS

<table>
<thead>
<tr>
<th>Problem</th>
<th>Remedial Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute dystonia</strong> (including oculogyric crises)</td>
<td>Give procyclidine 5-10 mg IM or benzatropine 1-2 mg IM</td>
</tr>
<tr>
<td></td>
<td>Procyclidine 1.25-2.5 mg in children</td>
</tr>
<tr>
<td><strong>Reduced respiratory rate</strong> (&lt;10/minute)</td>
<td>Given oxygen; raise legs; ensure patient is not lying face down</td>
</tr>
<tr>
<td>or oxygen saturation &lt;90%</td>
<td>Give flumazenil if benzodiazepine-induced respiratory depression suspected (see section 13)</td>
</tr>
<tr>
<td></td>
<td>If induced by any other sedative agent ventilate mechanically</td>
</tr>
<tr>
<td><strong>Irregular or slow pulse</strong> (&lt;50/minute)</td>
<td>Refer to specialist medical care immediately</td>
</tr>
<tr>
<td><strong>Fall in blood pressure</strong> (&gt;30mmHg orthostatic drop or &lt;50mmHg diastolic)</td>
<td>Lie patient flat; tilt bed towards head. Monitor closely</td>
</tr>
</tbody>
</table>

### 8.8 Guidelines for the Use of Clopixol Acuphase (zuclopenthixol acetate)

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

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

1.2 It is important to consider the pharmacokinetics of other drugs when prescribing it. For example, caution is necessary in a patient who has recently received a dose of a depot antipsychotic which has not yet reached peak levels.

1.3 Acuphase should only be given when enough time has elapsed to assess the full response of previously injected drugs. At least 15 minutes should be allowed after IV injections and 60 minutes after IM injections.

1.4 Acuphase should never be administered:

- in an attempt to ‘hasten’ the antipsychotic effect of any other antipsychotic therapy
- for treatment of acutely disturbed behaviour
- at the same time as other parenteral antipsychotics or benzodiazepines
- at the same time as depot medication
- as a ‘test dose’ for Zuclopenthixol
- to a patient who is unconscious
- to a patient who is physically resistive due to the risk of intravasation and oil embolus.
- to those with cardiac disease, hepatic or renal impairment or in pregnancy or under 12 years old
- to those who are sensitive to extrapyramidal side effects
- to those who the neuroleptic-naive

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

1.6 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 has no place in rapid tranquillisation: its action is not rapid.

1.7 Zuclopenthixol is a potentially toxic preparation with little evidence to support its use. It should therefore be avoided in acute episodes, unless specifically stated in the notes or in an advance directive that the patient responds best to this product.

8.9 NICE Clinical Guidelines


NICE defines Rapid Tranquillisation as the use of medication by the parenteral route (usually intramuscular or exceptionally, intravenous) if oral medication is not possible or appropriate and urgent sedation with medication is needed.

All staff that prescribe and administer the above medications should be:

- Aware of the risks associated with pharmacological management of acutely disturbed patients, such as:
  - damage to the therapeutic relationship between service user and Health Care Professional (NICE endorses requesting service users’ accounts of their experiences upon discharge to another unit)
  - over-sedation leading to loss of alertness and loss of consciousness (NICE guidelines mandate that the service user must be able to
respond to communication throughout and if verbal communication is lost, then the same level of care as for general anaesthesia must be used).

- cardiovascular and respiratory collapse [see monitoring after administration which consists of: temperature (risk of neuroleptic malignant syndrome), respiration rate, oxygen saturation, BP, HR (pulse), level of consciousness and any evidence of EPS. The physical and mental status of the service user should be taken into account in deciding the initial dose and subsequent dose increments.

- interaction of the medicines used in management with medicines already taken by the patient (whether prescribed by his/her GP, or illicit)

- Familiar with the medicines used in management, their correct prescription, and
  o that oral (PO) and intramuscular (IM) doses must be prescribed separately
  o that two drugs of the same class should not be written together (for example, do not write up diazepam and lorazepam, and/or haloperidol and olanzapine on the ‘prn’ side of the drug chart)
  o that medications should not be mixed in the same syringe (that is, lorazepam should be given by separate injection and site, from a concurrent haloperidol injection if combined antipsychotic/ benzodiazepine is clinically required)
  o the NEED FOR CONSENT, or else ensure that the appropriate Mental Health Section(s) is in place
  o the properties of drugs used– that is BNF and SPC requirements, including need for baseline ECG and the potential of individual drugs to lengthen (directly or indirectly) the QTc interval. Additionally they must know the total daily doses allowed and the need to titrate dose to effect.
  o the risks associated with particular classes of medicines:
    - Benzodiazepines: loss of consciousness; respiratory depression or arrest; cardiovascular collapse when receiving both clozapine and benzodiazepines
    - Antipsychotics: excessive sedation; loss of consciousness; cardiovascular/respiratory complications and collapse; seizures; akathisia; dystonia; dyskinesia; neuroleptic malignant syndrome
    - Antihistamines: excessive sedation; painful injection; additional antimuscarinic effects
  o the medicines NOT recommended, namely:
    - PO/IM chlorpromazine
    - IM diazepam
Thioridazine (no longer marketed in the UK)
IM depot antipsychotics
Olanzapine (for dementia-related disturbance)
Zuclopenthixol acetate due to long onset and duration of action. However, it may be considered as an option where there is a past history of good and timely response, or where there is an advance directive and when the service user has a history of disturbed behaviour over an extended time period.

- Aware that there are preferred levels of administration (the preferred method of drug administration being PO, then intramuscular IM and then, and only if immediate tranquillisation is essential, IV) and that:
  - if patient will accept oral and is not psychotic, NICE recommends oral lorazepam. Alternatively, if psychotic and taking oral, consider an antipsychotic (e.g. haloperidol or olanzapine) in addition to oral lorazepam.
  - if patient will not accept oral (or, from previous experience, this is considered ineffective) consider IM lorazepam for non-psychotic patients. Alternatively, if psychotic and not accepting oral, consider use of IM lorazepam in addition to IM antipsychotic (e.g. haloperidol or olanzapine).
  - IM Lorazepam and IM Olanzapine can only be given concurrently if a minimum of one hour has elapsed between the two agents (When using antipsychotics parenterally, ensure ready availability of parenteral procyclidine. NICE also recommends parenteral benztropine, but this product has, since, been discontinued in the UK.)

- Familiar with post management procedures, such as:
  - Regular monitoring and recording of BP, HR (pulse), RR, O2 saturations, level of consciousness, EPSE and temperature; the frequency of which must be increased if
    - IM/IV administration has been used
    - BNF/SPC dosages have been exceeded
    - High-risk situations such as known/suspected illicit drug use
    - Patient has a significant medical history/is on prescribed medication
  - If verbal responsiveness is lost – use same level of monitoring as for general anaesthesia
  - Upon transfer to another unit, ensure that full documentation is complete with:
    - Full medication history (that is, which medicines were/were not effective and any adverse drug interactions);
    - Formulation of advance directive(s);
    - Service user's account of their experience (if feasible).
References

9. College of Mental Health Pharmacy, haloperidol IM dose discussion topic, 17/1/2019.