Guidelines for the Use of Zuclopenthixol Acetate Injection

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Zuclopenthixol acetate (Clopixol Acuphase®) should not be prescribed where rapid sedation is required. It is not quick acting, is a potentially hazardous preparation with little published evidence to support its use in psychiatric emergencies and has the potential to be used inappropriately. In practical terms, zuclopenthixol acetate should be reserved for a minority of patients who have a prior history of its use.

Zuclopenthixol acetate should only be considered for the treatment of mania or psychosis where;

- the patient has had repeated injections of short-acting antipsychotics or benzodiazepines and sufficient time has elapsed to assess full response (at least 60mins after IM)
- giving further repeated injections of short-acting antipsychotics would be inappropriate
- it is known from the patient's history that they would otherwise require repeated injections of short-acting antipsychotics and the anticipated benefit of treating with zuclopenthixol acetate outweighs its risk
- patient has made an advance statement indicating this to be treatment of choice and the patient is known to have good tolerability and response

Zuclopenthixol acetate should only be prescribed under the instructions of a consultant psychiatrist.

A patient must be fully assessed by a doctor before each administration and under no circumstances should zuclopenthixol acetate be prescribed remotely.

Zuclopenthixol acetate should never be used;

- if immediate sedation is required (onset of action too slow)
- for patients who are accepting of oral antipsychotic medication
- in an attempt to hasten the antipsychotic action of other antipsychotics
- at the same time as other parental antipsychotics or benzodiazepines
- for patients who are antipsychotic naïve
- for patients who are sensitive to the extrapyramidal effects of antipsychotics
- for patients who have a history of Neuroleptic Malignant Syndrome
- for unconscious patients
- for patients who are pregnant or are breast-feeding
- for patients with Parkinson's disease or dementia with Lewy Bodies

Zuclopenthixol acetate should be used with extreme caution in patients;[1]

- with a history of cardiovascular disease or risk factors for QTc prolongation e.g. hypokalaemia, hypomagnesaemia
- who are known to have convulsive disorders, renal disorders, hepatic disorders or severe respiratory disease
- with pre-existing organic brain syndrome or learning disabilities or dementia
- who have risk factors for stroke
- with narrow angle glaucoma, prostatic hypertrophy, hypothyroidism, hyperthyroidism, myasthenia gravis, phaeochromocytoma
- who have used illicit substances or alcohol who are physically resistant due to risk of intravasation and subsequent oil embolism
- with concurrent prescriptions of drugs which increase zuclopenthixol levels e.g. fluoxetine and paroxetine

Dosing, onset and duration of action

- Zuclopenthixol acetate should be prescribed as a 'stat' dose only. If zuclopenthixol acetate is indicated, it should be administered immediately and not be prescribed 'just in case'.

- The lowest effective dose should be used to minimise adverse effects. The usual dose range is an intramuscular dose of 50-150mg (a Cochrane review suggests lower doses of 25-50mg are as effective as higher doses).[2] Lower doses should be used if patient tolerability is not known, in the elderly and in circumstances where caution is advised.

- Sedation may be apparent in a minority of patients around 2-4 hours after an injection of zuclopenthixol acetate, but antipsychotic action is evident only after 8 hours.[3] Peak serum concentrations of zuclopenthixol are usually reached 36 hours post injection, after which the serum levels decline slowly. The effects of a single injection can last up to 72 hours when the serum level is about one third of the maximum.[1]

- Where necessary and following assessment of mental and physical health, another injection may be administered after 48-72 hours. Some patients may need an additional injection between 24 and 48 hours after the first injection[1] although careful consideration of when peak plasma levels are likely to occur (around 36 hours) must be considered when contemplating repeat doses.

- The duration of treatment should not exceed 2 weeks and the cumulative dose must not exceed 400mg or 4 injections within a 2 week period.

- Zuclopenthixol acetate should never be viewed as a course of treatment. **The patient should be reviewed by a consultant psychiatrist before each dose is prescribed and administered.**

- Careful consideration should be given to the prescribing/administration of other antipsychotics and benzodiazepines following a dose of zuclopenthixol acetate (for at least 36 hours and up to 72 hours after each injection). The potential for inadvertent high dose antipsychotic therapy (HDAT) should be considered when prescribing zuclopenthixol acetate. High Dose Antipsychotic Guideline

Administration and monitoring post zuclopenthixol acetate

➢ **Administration**

- administration is by deep intramuscular injection into the upper outer buttock or lateral thigh

- great care should be taken, if patients are struggling excessively to resist injection, to avoid intravasation and oil embolism

- after administration, the patient should be closely monitored for potential adverse effects (see overleaf)

- duty doctor should be contacted if patient shows any abnormalities or concerns in observations

- adverse effects are generally dose dependent and more likely with no previous exposure

➢ Monitoring

<table>
<tr><th>Parameter</th><th>Frequency</th></tr>
<tr><td rowspan="3">The following parameters should be monitored, documented and scored using the NEWS tool

• Respiration
• Oxygen saturation
• Temperature
• Blood pressure
• Heart rate
• Level of alertness</td><td>Up to 36 hours post injection, monitoring should be hourly</td></tr>
<tr><td>From 36-72 hours post injection, monitoring can be decreased to every 4 hours if there are no concerns regarding the patient's physical status.</td></tr>
<tr><td>Consider increased monitoring if the individual;
• is asleep or oversedated
• has taken illicit drugs or alcohol
• has a pre-existing physical health problem
• has experienced any harm as a result of any restrictive intervention[4]</td></tr>
<tr><td colspan="2">Record and score all observations on NEWS. Escalate if necessary according to NEWS actions and escalation recommendations.</td></tr>
<tr><td>Extrapyramidal side effects</td><td>Monitor for acute dystonic reactions and administer IM procyclidine if necessary.</td></tr>
<tr><td>Fluid balance</td><td>Use fluid balance monitoring sheet to ensure adequate hydration, avoid fluid overload. Obtain U&Es where clinically appropriate.</td></tr>
<tr><td>Observation status</td><td>Ensure the patient is observed WITHIN EYE SIGHT by trained staff.</td></tr>
</table>

Where the patient refuses physical observations or remains too disturbed to obtain physical observations, consideration should be given to using the Visual Post IM Monitoring Form in Appendix 4 of the current NHSL Guideline for Intramuscular Medication for Acute Behavioural Disturbance in MH&LD inpatient services [6] **This should be used to monitor key physical observations according to the frequency described above and only where full monitoring cannot be managed for risk reasons or where the patient refuses.**

For management of potential problems occurring during the use of zuclopenthixol acetate, refer to table 5 in the current NHSL Guideline for Intramuscular Medication for Acute Behavioural Disturbance in MH&LD inpatient services [6]

A post-incident debrief involving both patient and staff members should take place at the earliest opportunity following the use of IM zuclopenthixol acetate (if clinically safe to do so).

Evidence base for zuclopenthixol acetate

BAP[3]

- Zuclopenthixol acetate is not recommended for use as rapid tranquillisation (RT) as the evidence does not support it even when BNF dose limits have been exhausted for other more commonly used drugs in RT, particularly as its onset of action takes several hours. However, after other strategies have failed to achieve a required response, its use may be considered as this may result in less numerous injections. **A baseline ECG is advised before use due to the risk of QTc prolongation.**

Cochrane[2]

- there is no suggestion that zuclopenthixol acetate is more effective than 'standard care' in controlling aggressive/disorganised behaviour, acute psychotic symptoms or preventing adverse effects
- lower doses of zuclopenthixol may be sufficient as no statistical difference was found in Brief Psychiatric Rating Scale (BPRS) outcomes between high and low doses.

RCPsych Consensus Statement[5]

- quotes the Cochrane review's identification of lack of evidence supporting its use and states that it is no longer recommended for rapid tranquillisation.
- it has been noted that a number of sudden deaths and fatal cardiac events have been reported to the Medicines Control Agency (MCA)/Medicines and Healthcare Products Regulatory Agency (MHRA) in relation to zuclopenthixol acetate.
- although there is little evidence to support its use some clinicians advocate the use of zuclopenthixol acetate with the rationale that the greater duration of action might reduce the need for repeated traumatic injections

The updated NICE guidance NG 10 makes no reference to the use of zuclopenthixol acetate.[4]

References

1. Clopixol Acuphase Solution for Injection 50mg/ml Summary of Product Characteristics. Last updated 26/1/17 www.medicines.org.uk accessed online 13/2/20

2. Cochrane Database of Systematic Reviews 18.4.2012, Issue 4. Art. No.: CD000525. Jayakody K, Gibson RC, Kumar A, Gunadasa S. Zuclopenthixol acetate for acute schizophrenia and similar serious mental illnesses

3. Patel et al. Joint BAP NAPICU evidence-based consensus guidelines for the clinical management of acute disturbance: De-escalation and rapid tranquillisation. Journal of Psychopharmacology 2018;1-40

4. NICE guideline. Violence and aggression: short-term management in mental health, health and community settings (NG10). May 2015 www.nice.org.uk/guidance/ng10

5. Royal College of Psychiatrist College Report. Consensus statement on high-dose antipsychotic medication. CR 190. November 2014

6. NHSL Guideline for Intramuscular Medication for Acute Behavioural Disturbance in MH&LD inpatient services Aug 2019