MONOGRAPH

Zuclopenthixol Acetate

This monograph only covers zuclopenthixol acetate (Clopixol Acuphase®) and must not be confused with zuclopenthixol decanoate (Clopixol Depot®), a long-acting intramuscular antipsychotic injection used for maintenance therapy.

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Zuclopenthixol is a high potency typical (first generation) antipsychotic. (1-3)

Zuclopenthixol acetate is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

- Acute and chronic psychoses (e.g. schizophrenia). (2, 3)
- Bipolar disorder (acute mania). (2-4)
- Highly agitated and aggressive patients. (3)

For use under the direction of a psychiatrist. See Formulary One.

CONTRAINDICATIONS

- Hypersensitivity to zuclopenthixol, thioxanthenes, or any component of the formulation. (1)

- Zuclopenthixol acetate **should never be administered**:
  - To 'hasten' the antipsychotic effect of other antipsychotic therapy. [5, 6]
  - For rapid tranquillisation or acute sedation (onset of effect is too slow).[7]
  - At the same time as other parenteral antipsychotics or benzodiazepines (may lead to over-sedation which is difficult to reverse).
  - As a 'test dose' for zuclopenthixol decanoate depot.[7]
  - To patients who are acutely intoxicated with alcohol, opiates, or barbiturates.[1]
  - To patients who have CNS depression (including reduced level of consciousness), suspected or established subcortical brain damage and circulatory collapse.[1]
  - To patients who have leukopaenia, blood dyscrasias and/or previous agranulocytosis[8]
  - To patients with phaeochromocytoma.[8]
  - To patients who accept oral medication.[7]
  - To patients who are neuroleptic-naïve (risk of prolonged extrapyramidal side effects [EPSE]) or sensitive to EPSE.[7]
  - To patients who are pregnant.[5, 8]

PRECAUTIONS [2]

- Respiratory failure – may cause respiratory depression.
- Hyperthyroidism – increases risk of acute dystonia.
- Temperature regulation – increased risk of hypo and hyperthermia.
- Gastrointestinal obstruction – may be exacerbated.
- Bladder obstruction – may be exacerbated.
- Myasthenia gravis – may be exacerbated.
- Diabetes – can increase blood glucose levels.
- Prolactinoma – can increase growth.
- Parkinson's disease – may aggravate condition.
- Lewy body dementia – can cause deterioration of motor and cognitive function.
- Epilepsy – can increase risk of seizures.
- Cardiovascular – can increase QT interval, increasing risk of arrhythmia.
- Blood pressure – can cause or worsen orthostatic hypotension.
- Thromboembolism – can increase the risk.
- Surgery – Reduced doses of anaesthetics and central nervous system depressants might be necessary.
- Patients who are physically resistant – risk of intravasation and oil embolism.[7]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- Zuclopenthixol Acetate 50 mg/mL ampoule

DOSAGE & DOSAGE ADJUSTMENTS

Zuclopenthixol acetate is seldom used in the paediatric population as there is limited safety and efficacy data and it poses a significant risk of causing extrapyramidal side effects and QTc prolongation.[2, 9, 10] It must only be prescribed by a psychiatrist for acutely psychotic or agitated patients when other conventional medications have failed or the patient has required repeated injections of short acting psychotropics.[7]

Zuclopenthixol acetate should be given only when enough time has elapsed to assess the full response to previously injected antipsychotic or benzodiazepine medications; allow 15 minutes after intravenous injections and 60 minutes after intramuscular injections.[7]

Intramuscular injection, **children > 12 years**: 25 - 50 mg initially, up to doses of 100 mg every 2 to 3 days.[11] If required, an additional dose can be given with a minimum interval of 24 hours following the first dose.[8] Maximum of 3 doses per course (up to 300 mg) over a 2-week period.[11]

Zuclopenthixol Acetate must be prescribed in the ONCE ONLY section of the paediatric Hospital Medical Chart (pHMC). All other parenteral antipsychotics must be withheld for 24 hours following administration of zuclopenthixol acetate, including PRN antipsychotics prescribed on the pHMC or Agitation and Arousal Medication Chart. If needed, IM benzodiazepines can be used with caution. [5, 6, 11]

Consider co-prescribing benzatropine particularly when the patient is at high risk of acute dystonia, and when their mental state is such that they will have difficulties communicating symptoms of dystonia. [2, 6, 11]

Hepatic impairment:

- Use with caution and consider dose reduction as zuclopenthixol undergoes extensive hepatic metabolism. [1, 2]

Renal impairment:

- No dosage requirements required. Use with caution. [1, 2]

Genetic factors:

- Zuclopenthixol is a major substrate of liver cytochrome P450 (CYP) enzyme 2D6. Genetic polymorphism of the CYP 2D6 enzyme occurs in some people. Consideration of dosage adjustment may be appropriate where genetic polymorphism is confirmed or suspected. [12, 13]

ADMINISTRATION

Intramuscular Injection:

- Inject into a large muscle (usually gluteal).[14]
- See Intramuscular (IM) Injections.

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Only commonly used drugs are listed below. This is not a complete list of incompatible drugs.

INCOMPATIBILITY:

Sesame oil. [14]

MONITORING

After giving intramuscular injection, commence 1:1 nursing observations of patient and document on the Observation and Response Tool. Escalate to medical referral as appropriate:

- Every endeavour should be made to have an ECG performed at baseline, 24 hours and 48 hours post-injection, when possible, to check for QT prolongation, particularly with concomitant treatment with other antipsychotics. [5]
- Vital observations (blood pressure, heart rate, respiratory rate, oxygen saturation and body temperature) at:
    - 15-minute intervals in the initial hour after administration of IM zuclopenthixol acetate, then hourly for the next 3 hours, then 2 hourly for the next 4 hours. Continue monitoring vital signs 4 hourly until 48 hours has lapsed since the dose was given. [5]
    - The above-mentioned requirements are summarised in the table below: [5]

Check Vital Observations at the Following Times Post Zuclopenthixol Acetate Administration
15 minutes
30 minutes
45 minutes
60 minutes

2 hours
3 hours
4 hours
6 hours
8 hours
12 hours
16 hours
20 hours
24 hours
28 hours
32 hours
36 hours
40 hours
44 hours
48 hours

- When patients are asleep (e.g. during the night), their respiratory function should be monitored on an hourly basis. (5)
- Attempts should be made to awaken the patient if there is evidence of respiratory distress or obstruction.(5)
    - A code blue should be initiated if the patient is difficult to rouse. (5)
- Fluid balance must be monitored to ensure adequate hydration levels. (5)
- Onset and duration of action:
    - Zuclopenthixol acetate's action is not rapid and sedative effects usually begin 2 hours after injection and peak at 12 hours. Maximum plasma concentration is reached at approximately 24-36 hours post-injection followed by a gradual decline. The effects may last for up to 72 hours. (1, 3, 7, 8, 15)

ADVERSE EFFECTS

Common: Sedation, anxiety, agitation, extrapyramidal side effects (EPSEs) [see below], orthostatic hypotension, tachycardia, blurred vision, mydriasis, constipation, nausea, dry mouth,

urinary retention, sexual adverse effects, weight gain, hyperprolactinaemia (may result in galactorrhoea, gynaecomastia, amenorrhoea or infertility). (2)

Infrequent or Rare: Allergic reactions (including urticaria),Stevens-Johnson syndrome, intra-operative floppy iris syndrome, syndrome of inappropriate anti-diuretic hormone secretion (SIADH), hyperthermia, hypothermia, neuroleptic malignant syndrome, anaemia, thrombocytopenia, neutropenia, agranulocytosis, venous thromboembolism, stroke, electrocardiogram (ECG) changes (reversible, broadened QT interval), arrhythmias, cardiac arrest, sudden death, hepatic fibrosis, priapism, systemic lupus erythematosus, seizures, increased blood glucose, dysarthria, dysphagia, new or worsening obsessive-compulsive symptoms. (2)

Extrapyramidal side effects:

- Akathisia – A feeling of motor restlessness. Usually occurs 2-3 days after starting treatment. (2)
- Parkinsonism – Includes tremor, rigidity or bradykinesia. Usually develops after weeks or months of treatment. (2)
- Tardive dyskinesia – Involuntary movements of the face, mouth, tongue, and sometimes head and neck, trunk or limbs. Usually occurs after medium to long term treatment. (2)
- Dystonias - An involuntary contraction of major muscle groups that is highly disturbing to the patient. These include torticollis, carpopedal spasm, trismus, perioral spasm, laryngeal spasm (may be life threatening), opisthotonos and oculogyric crises.(2)

Acute dystonia often occurs within 24-48 hours of starting treatment but can occur throughout the treatment course.(2) Other risk factors for dystonia include young age, male sex, use of cocaine and a history of acute dystonic reactions. (2)

Consider co-prescribing benzatropine particularly when the patient is at high risk of acute dystonia, and when their mental state is such that they will have difficulties communicating symptoms of dystonia. (2, 6, 11)

Neuroleptic malignant syndrome:

- A potentially fatal condition characterised by fever, marked muscle rigidity, altered consciousness and autonomic instability; usually progresses rapidly over 24-72 hours. (2) Elevation of serum creatinine kinase concentration (skeletal muscle origin) and leucocytosis often occur. There is a higher incidence of occurrence in young males.(2)

STORAGE

- Store below 25°C.(8)
- Protect from light. Do not remove from carton except immediately prior to use.(8)

INTERACTIONS

Zuclopenthixol is a substrate of CYP 2D6 (major) [1, 8], and 3A4 (minor) [1]. Care must be taken when co-prescribing medications that inhibit these enzymes (e.g. fluoxetine and fluvoxamine) as this can lead to significantly higher serum levels of zuclopenthixol.[1, 8]

This medication can prolong QT interval[1] and may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **zuclopenthixol acetate**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

- CAHS Medication Management Guideline: Arousal and Agitation Drug Management
- Intramuscular (IM) Injections

Related external legislation, policies and guidelines

- Psychotropic Medication: Physical Health Monitoring Handbook CAHMS
- CAMHS Monitoring the effects of psychotropic medication on physical health policy
- CAMHS Antipsychotic Physical Health Monitoring Form

References

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Useful resources (including related forms)
Zuclopenthixol Acetate - Clopixol Acuphase® Guideline
Consent for Off-label Medication Use Form
Clopixol® Acuphase Patient Information Leaflet

This document can be made available in alternative formats on request for a person with a disability.

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