Specialised Medicines Service Guideline ~ Zuclopenthixol decanoate injection for schizophrenia and paranoid psychoses in adults

This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to the BNF and individual product SPCs for full prescribing data.

Specialist: Please complete letter at the end of this document and send together with the shared care guideline to the GP.

GP: Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.

GPs are invited to participate. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Introduction and aims of treatment

This guideline only applies to patients registered with GP practices in Devon, and for whom Devon Partnership Trust (DPT) is the secondary care provider of mental health services.

This guideline does not apply to patients for whom Livewell Southwest is the secondary care provider of mental health services.

Zuclopenthixol decanoate injections are prescribed to support adherence with antipsychotic medication.

This guideline refers only to the use of zuclopenthixol decanoate injections for the maintenance treatment of schizophrenia and paranoid psychoses, in adults aged 18 years and older. Other (unlicensed) indications are outside the scope of this guideline.

Zuclopenthixol acetate injection is outside the scope of this guideline.

Important: Zuclopenthixol decanoate has been confused with zuclopenthixol acetate; care must be taken to ensure the correct drug is prescribed and dispensed.

NICE clinical guideline CG178 (Psychosis and schizophrenia in adults: prevention and management) states that GPs and other primary healthcare professionals should monitor the physical health of people with psychosis or schizophrenia when responsibility for monitoring is transferred from secondary care, and then at least annually. The health check should be comprehensive, focusing on physical health problems that are common in people with psychosis and schizophrenia (refer to the NICE clinical guideline for further information).

This Specialised Medicines Service prescribing guideline details drug specific additional monitoring requirements over and above those recommended by NICE for all patients with psychosis or schizophrenia.

Specialist responsibilities

Consultants may decide to delegate some of these tasks to members of their team; however, the responsibility for ensuring the following are undertaken remains with the consultant:

- Assess the patient, establish a diagnosis and agree a management plan
- Undertake monitoring of parameters (at baseline and during titration period) and communicate these to GP on transfer of care (see monitoring schedule, below)
- Update records with list of existing drugs from available resources and ensure that there are no drug interactions with current medication
- Discuss benefits and side effects of treatment (including risk of developing tardive dyskinesia) with patient and carer to enable an informed choice to be made, including provision of information leaflets where available
- Initiate treatment and titrate dose; establish patient on a stable dose and administration frequency
- Continue prescribing and administering until GP indicates agreement to accept transfer of prescribing and administration responsibilities
- Write to the GP once the condition of the patient is sufficiently stable for transfer into primary care, include details of who to contact in the case of non-attendance for depot injection
- Transferring of **prescribing, administration, and drug safety monitoring** must only occur once the person is assessed as stable by the specialist service (usually not less than 3 months following initiation). The nurse who previously administered the injection is responsible for ensuring the primary care nurse is competent to administer the depot and facilitate training via demonstration if necessary.
- Ensure full prescribing details are provided (strength, dose, volume per injection that the patient has been receiving to date, the need for multiple injections to administer the dose etc.)
- Ensure that the recovery co-ordinator has drawn up a care plan involving the GP, that details who is responsible for administration of injections, and where; and ensure that suitable storage facilities are available, and injection is available at appropriate time; this should also detail what contingency is in place in the case of an individual's non-attendance for depot injection
- Ensure that the GP is informed in writing of any changes in the patient's care team or their contact details
- Discuss discontinuation of treatment with the patient when appropriate; advise the GP on when and how to discontinue treatment if necessary and agree a plan (including specialist supervision where appropriate)
- Report any adverse events to MHRA via Yellow Card Scheme
- Evaluate any adverse effects reported by GP and identification of specific monitoring required
- Advise GP on any alteration of dose according to clinical parameters
- Be accessible for any support that the GP may require with respect to the individual's care.
- Continue to review the patient at agreed specified clinically appropriate intervals (including response to treatment and need to continue therapy), sending a written summary to the GP whenever the patient is reviewed, including the current dose to be prescribed

The secondary care team will maintain responsibility for **monitoring the patient's physical health and the effectiveness of antipsychotic medication** for the first 12 months or until the person's condition has stabilised, whichever is longer.

General practitioner responsibilities

GPs may decide to delegate some of these tasks to members of their team; however, the responsibility for ensuring the following are undertaken remains with the GP:

- Ensure a timely reply is sent to specialist in response to request for sharing of care.

If GP has agreed to share care:

- Prescribe and administer zuclopenthixol decanoate injection in line with agreed treatment plan
- Zuclopenthixol decanoate has been confused with zuclopenthixol acetate (outside the scope of this guideline); care must be taken to ensure the correct drug is prescribed and dispensed.
- Ensure that the practice nurse has received relevant training and is competent to administer the depot injection; if they have not, advice and training should be sought from the specialist team
- Follow specialist advice on any changes in treatment
- Liaise with Community Mental Health Team regarding follow up in the event of non-attendance, in line with individual details provided in the original request to share care (see below)
- Monitor the patient's overall health and wellbeing. Report and seek advice from specialist on any aspect of patient care which is of concern to GP
- Ask the patient about side effects at every contact
    - If patient reports symptoms of hyperprolactinaemia (see below), check prolactin levels and seek specialist advice (depot can be administered in the meantime)
    - If patient reports general "low level" movement disorders (tremor, stiffness, abnormal/unusual movements) seek specialist advice (depot can be administered in the meantime)
    - If patient reports symptoms of acute dystonia (neck twisting, eyes protruding/rolling back into head, tongue protruding etc.), **do not administer depot**, seek same day GP review (and urgent specialist advice)
- Seek specialist advice if:
    - Intolerable side effects
    - New or increased comorbid substance misuse
    - Increased risk to self or others
    - The individual's mental health presentation changes significantly
    - The individual expresses a desire to stop their treatment
- Discontinue treatment on advice from specialist, ensuring a clear management plan is agreed with the specialist
- Inform specialist of all relevant medical information regarding the patient, including adverse effects
- Ensure there are no drug interactions with existing drugs and be alert to the possibility of interactions (or additive risk of side effects) when initiating new drugs.

Symptoms of hyperprolactinaemia

Men: reduced libido, erectile dysfunction, gynaecomastia, or galactorrhoea

Women: irregular/infrequent periods or amenorrhoea, galactorrhoea, hirsutism, or reduced libido

Monitoring

NICE clinical guideline CG178 states that primary care should monitor the physical health of people with psychosis or schizophrenia when responsibility for monitoring is transferred from secondary care, and then at least annually (refer to the NICE clinical guideline for further information).

This physical health monitoring is outside the scope of this Specialised Medicines Service (SMS) prescribing guideline, which details drug specific additional monitoring requirements over and above those recommended by NICE for all patients with psychosis or schizophrenia. Physical health monitoring is the subject of a separately commissioned LES.

Assessment to be completed by the specialist service provider at baseline:

- Prolactin levels
- Assessment of any movement disorders
- Electrocardiogram (ECG) where necessary

Ongoing drug safety monitoring to be completed by the GP/nurse:

- Ask the patient about side effects at every contact
    - If patient reports symptoms of hyperprolactinaemia (see above), check prolactin levels and seek specialist advice (depot can be administered in the meantime)
    - If patient reports general "low level" movement disorders (tremor, stiffness, abnormal/unusual movements) seek specialist advice (depot can be administered in the meantime)
    - If patient reports symptoms of acute dystonia (neck twisting, eyes protruding/rolling back into head, tongue protruding etc.), **do not administer depot**, seek same day GP review (and urgent specialist advice)

Patient responsibilities

- Tell the GP or specialist if they have any concerns or do not understand any aspect of treatment
- Attend specialist, GP, practice nurse and blood test appointments
- Tell the doctor or nurse if they experience any of following symptoms of hyperprolactinaemia:
    - **Men**: reduced libido, erectile dysfunction, gynaecomastia, or galactorrhoea
    - **Women**: irregular/infrequent periods or amenorrhoea, galactorrhoea, hirsutism, or reduced libido
- Tell the doctor or nurse if they experience any movement related side effects such as tremor, stiffness, abnormal or unusual movements
- Report any other side effects to the doctor or nurse
- Patients and/or carers should monitor for any clinical worsening and seek medical advice if these symptoms occur
- Seek medical attention if they become acutely ill for any reason
- Talk to their doctor as soon as possible if they become pregnant or are planning a pregnancy
- Tell their community pharmacist that they are being treated with zuclopenthixol decanoate injection when buying any over-the-counter medicine.

Supporting Information

Please refer to individual product SPCs for full prescribing data; these can be accessed at www.medicines.org.uk.

Dosage and administration

Refer to the current BNF and individual product SPC

Zuclopenthixol decanoate has been confused with zuclopenthixol acetate; care must be taken to ensure the correct drug is prescribed and dispensed.

Administered by deep intramuscular injection into the upper outer buttock or lateral thigh. As with all oil-based injections it is important to ensure, by aspiration before injection, that inadvertent intravascular entry does not occur.

In general not more than 2–3 mL of oily injection should be administered at any one site. Correct injection technique (including use of z-track technique) and rotation of injection sites are essential.

Treatment is usually started with a small dose to assess tolerability, with subsequent doses adjusted according to response. This initiation and titration will be undertaken by the specialist.

The usual maintenance dosage of zuclopenthixol decanoate lies between 200 mg to 500mg every one to four weeks, but some patients may require up to 600 mg weekly. The maximum single dose at any one time is 600 mg. Patient specific guidance will be provided to the GP by the specialist.

Dose adjustments may be required in frail or elderly patients; and those with hepatic impairment or renal failure – seek specialist advice.

Contraindications and precautions

Refer to the current BNF and individual product SPC

Contraindications: circulatory collapse; CNS depression; comatose states; phaeochromocytoma; children

Caution should be exercised in patients having: liver disease; cardiac disease, or arrhythmias; severe respiratory disease; renal failure; epilepsy (and conditions predisposing to epilepsy, e.g. alcohol withdrawal or brain damage); Parkinson's disease; narrow angle glaucoma; prostatic hypertrophy; hypothyroidism; hyperthyroidism; myasthenia gravis; and patients who have shown hypersensitivity to thioxanthenes or other antipsychotics.

Zuclopenthixol should be used with caution in patients with risk factors for stroke.

zuclopenthixol decanoate may modify insulin and glucose responses calling for adjustment of the antidiabetic therapy in diabetic patients.

Pregnancy and lactation

Refer to individual product SPC. Seek specialist advice.

Zuclopenthixol decanoate should not be administered during pregnancy unless the expected benefit to the patient outweighs the theoretical risk to the foetus.

As zuclopenthixol is found in breast milk in low concentrations it is not likely to affect the infant when therapeutic doses are used. Breast-feeding can be continued during zuclopenthixol decanoate therapy

if considered of clinical importance, but observation of the infant is recommended, particularly in the first 4 weeks after giving birth.

Effects on ability to drive and use machines

Refer to individual product SPC

Zuclopenthixol decanoate is a sedative drug. Alertness may be impaired, especially at the start of treatment, or following the consumption of alcohol; patients should be warned of this risk and advised not to drive or operate machinery until their susceptibility is known. Patients should not drive if they have blurred vision.

Adverse effects

Refer to individual product SPC

The majority of undesirable effects are dose dependent. The frequency and severity are most pronounced in the early phase of treatment and decline during continued treatment.

Neuroleptic malignant syndrome (a rare but potentially fatal idiosyncratic response characterized by hyperthermia, generalised muscle rigidity, autonomic instability, altered consciousness and increased serum creatine phosphokinase levels). Hyperthermia is often an early sign of this syndrome. Antipsychotic treatment must be withdrawn immediately and appropriate supportive therapy and careful monitoring instituted.

Rare cases of QT prolongation, ventricular arrhythmias (ventricular fibrillation, ventricular tachycardia), Torsade de Pointes, and sudden unexplained death have been reported for zuclopenthixol.

Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic drugs (Frequency unknown).

Drug interactions

This list is not exhaustive, for additional information, and further interactions, consult the current BNF and individual product SPC.

The following drug interactions are classified in the online version of the BNF as **severe** (the result may be a life-threatening event or have a permanent detrimental effect):

- Zuclopenthixol is predicted to decrease the effects of **levodopa**. Manufacturer advises avoid or monitor worsening parkinsonian symptoms
- Zuclopenthixol potentially increases the risk of neurotoxicity when given with **lithium**
- Zuclopenthixol **prolongs the QT interval**; most manufacturers advise avoiding the use of two or more drugs that are associated with QT prolongation. Increasing age, female sex, cardiac disease, and some metabolic disturbances (notably hypokalaemia) predispose to QT prolongation. A large number of drugs are highlighted in the BNF as interacting in this way with zuclopenthixol
- The risk of **Torsade de Pointes** is predicted to increase when zuclopenthixol is given with a large number of other drugs (Manufacturer advises use with caution or avoid) – refer to BNF.
- Zuclopenthixol is predicted to decrease the effects of **histamine**. Manufacturer advises avoid.

The following drug interactions are classified in the online version of the BNF as **moderate** (the result could cause considerable distress or partially incapacitate a patient; they are unlikely to be life-threatening or result in long-term effects):

- Zuclopenthixol is predicted to decrease the effects of **amantadine**; **apomorphine; bromocriptine; pergolide; quinagolide; ropinirole;** and **rotigotine.** Manufacturer advises avoid.

Support

Contact details	
Devon Partnership NHS Trust	Individual contact details for the patient's recovery co-ordinator will be provided in the original request to share care Trust HQ (Wonford House reception): 01392 208866 Emergency Duty Team: 0345 6000 388 (outside office hours) Single point of access for referral: 0300 5555 000 (Option 1, option 3) Single point of access email: dpt.spa@nhs.net

Date ratified: February 2020 (updated single point of access contact details 8th July 2020)

Shared Care Agreement Letter - Consultant Request

To:	**Dr:**
	Practice Address:
	Patient Name:
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition: ……

I recommend treatment with the following drug: ……

At the following dosage: ……..……

I request your agreement to continue the care of this patient according to the Specialised Medicines Service Guidelines for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Specialised Medicines Service Guidelines.

The results of any relevant baseline tests and any additional supportive information (target range, date of last blood test etc.) are included below:

Non-attendance for injection or other concerns

If the above-named patient does not attend an appointment for depot drug administration, or you have any other concerns please contact their recovery co-coordinator for advice:

Recovery co-ordinator name: ……

Recovery co-coordinator direct telephone: …….

Team telephone number: ……...

Team email address: ……..

If you are unable to contact the recovery co-ordinator, or their team, contact the trust switchboard on 01392 208866

Principles:
GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are under no obligation to do so.** If so, the clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:		**Date:**
Consultant name:		
Telephone number:		
Email address		

Please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Specialised Medicines Guideline.

Signed: …….. Date: …….

GP name: ……. *Delete as appropriate.

Patient agreement

I understand and agree to my responsibilities as described above.

Signed: ……... Date: …….

Name: …….