NHS Greater Glasgow & Clyde
Mental Health Services
Prescribing Management Group

Guidance for use of olanzapine embonate long-acting injection (Zypadhera) in GGC

1. Background

Olanzapine Long-Acting Injection (Zypadhera®) is indicated for the maintenance treatment of adult patients with schizophrenia whose condition has been sufficiently stabilised during acute treatment with oral olanzapine and who have been assessed as having adherence problems with long-term oral medication.

Olanzapine LAI has a side effect profile similar to oral olanzapine but does carry a small but significant risk of post-injection syndrome, therefore patients must be monitored in a healthcare facility by an appropriate healthcare professional for 3 hours after the administration of each injection.

2. Scope

This guideline gives advice to prescribers and other healthcare professionals on the use of olanzapine embonate (LAI) and appropriate monitoring of patients following administration.

3. Before prescribing

- Olanzapine LAI has not been accepted for use by the Scottish Medicines Consortium (SMC) therefore is non-formulary. Requests will be considered by the Prescribing Management Group for Mental Health (PMG-MH). PMG-MH authorization through the Peer Approved Clinical System (PACS2) is required prior to prescribing
- Consideration must be given to which healthcare facility the patient will receive the injection (both in the short and longer term). There must be clear communication and agreement with community services that there is adequate measures in place for future administration
- If the patient is subject to a Compulsory Treatment Order under the Mental Health (Care&Treatment) (Scotland) Act 2003, olanzapine LAI must be specified on the T2/T3B form
- Clinical considerations – for further prescribing information please refer to the most up to date summary of product characteristics for Zypadhera®
- Patient criteria:
    - A medication history should be completed by pharmacy to ensure the patient meets the criteria for use of olanzapine embonate LAI i.e. the patient must require treatment with depot medication and previous trials of both a typical depot and Risperidone OR Paliperidone OR Aripiprazole LAI must have been unsuccessful
    - Must have a history of response and tolerability to oral olanzapine
    - Must be advised of the risk of post injection syndrome, information leaflet available on choice and medication

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- Due to the risk of post injection syndrome, they must be advised of the need for them to be observed in a healthcare facility for three hours after each injection

4. Dose

Target oral olanzapine dose	Recommended starting dose of ZYPADHERA	Maintenance dose after 2 months of ZYPADHERA treatment
10 mg/day	210 mg/2 weeks or 405 mg/4 weeks	150 mg/2 weeks or 300 mg/4 weeks
15 mg/day	300 mg/2 weeks	210 mg/2 weeks or 405 mg/4 weeks
20 mg/day	300 mg/2 weeks	300 mg/2 weeks

In renal or hepatic impairment, a lower starting dose should be considered (e.g. 150mg every 4 weeks).

5. Administration

Olanzapine LAI should only be administered by deep intramuscular gluteal injection by a healthcare professional trained in the appropriate injection technique.

All staff involved in the administration must undertake the training resources available on the Zypadhera® website (registration required). A signed and dated printed copy of the company training material should be returned to their manager to confirm completion.

Once reconstituted, olanzapine LAI should be used immediately. However, if not used right away it will retain efficacy for up to 24 hours at room temperature and will re-suspend if shaken vigorously. Any olanzapine LAI that has been reconstituted for longer than 24 hours must be discarded.

6. Monitoring

Pre-administration

It should be confirmed that the patient is alert and does not appear sedated prior to administering olanzapine LAI.

Temperature, pulse, respiratory rate (TPR) and blood pressure (BP) are required to be monitored and recorded on a NEWS observation chart/EMIS prior to each administration of olanzapine LAI.

Post-administration

After **each** injection, patients should be observed in a healthcare facility by appropriately qualified personnel for at **least 3 hours** for signs and symptoms consistent with olanzapine post injection syndrome.

After administration, the patient must be checked **every 15 minutes for the first hour**, thereafter, **every 30 minutes for a further 2 hours**. The patient's level of consciousness and orientation to time and place should be assessed and ensure they are not displaying any symptoms of post-injection syndrome (see section 7). This should be recorded after each administration on the observation record chart (appendix 1) and an entry made within the patients EMIS record.

After 3 hours, post-injection syndrome is unlikely to occur. Out-patients may be allowed to return home if:

- It is confirmed that the patient is alert, orientated and absent of any signs and symptoms of post injection syndrome
- They travel to their destination accompanied by someone
- They know they must not drive or operate machinery for the rest of that day

7. Post-injection syndrome

- Post-injection syndrome is related to excessive olanzapine plasma concentrations caused by unintended partial intravascular injection and occurs in a small number of people (less than 1 in 1400 injections), even with appropriate injection technique
- Median time to onset of symptoms within 25 minutes
- Post-injection syndrome is seen within one hour of injection in 80% of cases
- If post-injection syndrome is not evident within one hour, it rarely occurs within 1 to 3 hrs (less than 1 in 7000 injections) and very rarely after 3 hours (less than 1 in 10000)
- In all cases full recovery was reported to have occurred within 24 to 72 hours after the injection
- For further information on the treatment of olanzapine overdose refer to the Toxbase database (log in required)

Symptoms of post-injection syndrome are consistent with olanzapine overdose and typically include:

- Sedation (ranging from mild to severe)
- Delirium (disorientation and cognitive impairment)
- Confusion
- Dysathria (slurred speech)
- Ataxia
- Agitation
- Anxiety
- Hypertension
- Dizziness
- Movement disorders or EPSE
- Seizure activity

If the patient displays any symptoms of post-injection syndrome, medical advice should be sought immediately and vital sign monitoring commenced:

Temperature, pulse, respiratory rate, oxygen saturations and blood pressure should be monitored every 15 minutes for 90 minutes after symptoms of post-injection syndrome develop. Thereafter, monitor these signs every 30 to 60 minutes until symptoms resolve.

Medical staff should determine where the most appropriate setting for continued monitoring is.

Trigger points for concern may include:

- Progressive sedation levels with reduced consciousness
- Respiratory rate reduction to 10 breaths/minute
- Irregular or slow pulse < 50/min
- Rapid pulse increase
- Fall in BP < 80mm Hg systolic or < 50mm Hg diastolic
- Increased temperature
- Development of cyanosis

If post-injection syndrome occurs:

- Immediately call for medical assistance
- Dial 999
- Give supportive care
- A&E staff should be informed of the olanzapine LAI administration

If parenteral benzodiazepines are essential for the management of post injection adverse reactions, careful evaluation of clinical status for excessive sedation and cardiorespiratory depression is recommended.

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Appendix 1- Olanzapine LAI Observation Record Chart (please complete for each administration)

Patient Name: _____ CHI: _____
Date and Time of Administration: _____
Ward: _____

Pre-injection

Patient alert and ambulatory (able to walk about) YES/NO
Temperature, pulse, respiration rate and blood pressure documented on NEWS chart/EMIS YES/NO

Post- Injection

Time	Conscious level (see below)	Orientated to time/place: Y/N	Post Injection Syndrome – signs / symptoms. See below. Y / N	Staff signature
Pre-injection				
15 mins				
30 mins				
45 mins				
1 hour				
1.5 hours				
2 hours				
2.5 hours				
3 hours				

Conscious level assessment:

1. Awake and active
2. Awake but calm
3. Asleep but rousable
4. Asleep and unrousable

Post injection syndrome – Signs and Symptoms:

- Delirium (Confusion, aggression, agitation, anxiety, disorientation)
- Extrapyramidal side effects, cramps in extremities
- Difficulty with tongue or lip movements or slurred speech. Difficulty with balance, walking, speaking, swallowing, eating or seeing
- Weakness / Dizziness
- High blood pressure or seizure activity

For any patient who scores 4 on the conscious level assessment or who shows signs/symptoms of Olanzapine Post Injection Syndrome, call 999 immediately. For non-urgent concerns contact on-call/duty doctor.

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