Olanzapine Long Acting Injection (LAI) Guideline

Guidance and Procedure for the use of Olanzapine LAI Hertfordshire Partnership University NHS Foundation Trust

Version: 1.2

Lead Author: Chief Pharmacist

Approved Date: 15th July 2019
Approved By: Drug and Therapeutics Committee

Issue Date: July 2019
Review Date: July 2021

Target Audience:
This guideline must be read and understood by staff working involved in prescribing and administering olanzapine LAI

1.0 Introduction/Background

Olanzapine LAI is a licensed medication for the maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine. The product gained a marketing authorisation in 2010, however its use in the United Kingdom is somewhat limited due to safety concerns and consequent monitoring requirements post administration.

2.0 Safety Concerns

During pre-marketing clinical studies, reactions that presented with signs and symptoms consistent with olanzapine overdose were reported in patients following an injection of olanzapine LAI. This "post injection syndrome" occurred in <0.1% of injections and approximately 2% of patients. Most of these patients developed symptoms of sedation (ranging from mild in severity up to coma) and/or delirium (including confusion, disorientation, agitation, anxiety and other cognitive impairment). Other symptoms noted include extrapyramidal symptoms, dysarthria, ataxia, aggression, dizziness, weakness, hypertension and convulsion. In most cases, initial signs and symptoms related to this reaction appeared within 1 hour following injection, and in all cases full recovery was reported to have occurred within 24 - 72 hours after injection. Reactions occurred rarely (<1 in 1,000 injections) between 1 and 3 hours, and very rarely (<1 in 10,000 injections) after 3 hours.

As a result of these adverse reactions, when discussing initiation, patients should be advised about this potential risk and must agree to the need to be observed for 3 hours in a healthcare facility each time olanzapine LAI is administered. Post-marketing reports of post-injection syndrome since the marketing authorization of olanzapine LAI are generally consistent with the experience seen in clinical studies.

3.0 Use within Hertfordshire Partnership University Foundation NHS Trust (HPFT)

Olanzapine LAI is **NOT** approved for routine use within HPFT primarily due to the safety concerns identified above. A non-formulary request **must** be made to the Drugs and Therapeutic Committee (DTC) by the Consultant for use on a patient by patient basis. For those patients maintained on olanzapine LAI who are transferred to HPFT, the treatment plan should be reviewed and if olanzapine LAI is considered to be drug of choice for that individual patient, a non-formulary request must be made to DTC by the Consultant.

Before considering prescribing olanzapine LAI, the Consultant must be assured that:

- Patients have a history of response and tolerability to oral olanzapine
- Patients have demonstrated adherence problems with long-term oral medication
- Patients have been advised about the potential risks of olanzapine LAI post-injection syndrome, the requirement for them to be observed for three hours in a healthcare facility after each administration of injection and that they should not drive or operate machinery for the rest of the day. If it is felt that the patient might not comply with these requirements, olanzapine LAI must not be initiated.
- A care plan has been agreed with the Consultant and nursing staff that will undertake the post administration observation within a healthcare facility in the community.

4.0 Prescribing Olanzapine LAI

- All patients must have a history of response and tolerability to oral olanzapine before olanzapine LAI is prescribed.
- Recommended dose scheme when transferring patients from oral olanzapine to olanzapine LAI is detailed below:

Target oral olanzapine dose	Recommended starting dose of Olanzapine LAI	Maintenance dose after 2 months of 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

- Olanzapine LAI is to be administered by deep intramuscular gluteal injection
- The maximum licensed dose of olanzapine LAI is 300mg 2-weekly or 405mg 4-weekly
- Patients should be monitored carefully for signs of relapse during the first one to two months of treatment
- Supplementation with oral olanzapine was not authorised in double-blind clinical studies. If oral olanzapine supplementation is clinically indicated, then the combined total dose of olanzapine from both formulations should not exceed the corresponding maximum oral olanzapine dose of 20 mg/day.
- Olanzapine LAI has not been studied in elderly patients and therefore is not recommended for this treatment population unless a well-tolerated and effective dose regimen using oral olanzapine has been established. A lower starting dose (150 mg/4 weeks) is not routinely indicated, but should be considered for those 65 and over when clinical factors warrant. Olanzapine LAI is not recommended to be started in patients >75 years.
- Olanzapine LAI is **not licensed** for use in patients aged less than 18 years of age
- In renal and hepatic impairment a lower starting dose (150 mg every 4 weeks) should be considered. In cases of moderate hepatic insufficiency (cirrhosis, Child-Pugh class A or B), the starting dose should be 150 mg every 4 weeks and only increased with caution.
- Clinicians prescribing olanzapine LAI must review the ZypAdhera Product Training Slides which are available through the manufacturers https://www.zypadhera.co.uk/SignIn.aspx

5.0 Administration

Due to the “post injection syndrome” adverse reactions described above, Olanzapine LAI must be administered by **deep intramuscular gluteal injection**:

- By a Dr or Nurse who have been trained in the administration of depot injection technique
- In a location where at least 3 hours of observation of the patient can take place
- Where rapid access to medical (or paramedical) care, if needed, (to include dialling 999 if a doctor is not on the premises), must be available throughout the observation period.

Post injection syndrome observation

The staff member undertaking the observation must be vigilant for any signs and symptoms consistent with olanzapine overdose such as:

- sedation and delirium (disorientation, confusion, agitation, anxiety and other cognitive impairment)
- extrapyramidal symptoms
- dysarthria (slurred speech)
- ataxia (staggering, uneven gait)
- aggression
- dizziness
- weakness
- hypertension
- convulsion

Post injection syndrome usually occurs within three hours of olanzapine depot. The risk of post injection syndrome does NOT decrease. It remains the same at EVERY injection. The three hour observation period should be extended as clinically appropriate for patients who exhibit any signs or symptoms consistent with olanzapine overdose, until signs/symptoms resolved.

Within HPFT the post injection monitoring of Olanzapine LAI can be undertaken by a nurse, nursing associate or health care assistant (HCA) however the HCA must be supported by a member of the nursing team as follows:

- The nurse administering the Olanzapine LAI and delegating the post injection syndrome monitoring to the HCA must have completed the online training available through the manufacturers https://www.zypadhera.co.uk/SignIn.aspx and read through this guidance document fully.
- Explain to the HCA the symptoms to be vigilant for that are consistent with olanzapine overdose (as above)
- Explain how to undertake the post injection syndrome observations and complete the monitoring form in Appendix 1.
- The nurse must be on site if the HCA has any queries/concerns/need to escalate issues

Following observation period

The nurse should discharge the patient and ensure that:

- Patients must be advised to be vigilant for signs and symptoms of olanzapine overdose (secondary to post-injection adverse reactions) for the remainder of the day following administration of olanzapine LAI.
- Assurance must be sought that they will remain in a position to obtain assistance if needed and that they will not drive or operate machinery.
- All patients must be issued with a copy of the Zypadhera® patient information card before they leave the unit / clinic if they are not already carrying one. The card contains important safety information for the patient on post-injection adverse events.

If the patient refuses to adhere to the post injection monitoring schedule it should be escalated to the Consultant in charge of the patient.

Hertfordshire Partnership NHS
University NHS Foundation Trust

Olanzapine LAI Post injection syndrome observation form

Patient name: **NHS/Paris number:** **D.O.B**

Name of nurse/nursing associate/HCA conducting observation:

Sign/Symptoms to observe: Sedation and delirium (disorientation, confusion, agitation, anxiety and other cognitive impairment), extrapyramidal symptoms, dysarthria (slurred speech), ataxia (staggering, uneven gait), aggression, dizziness, weakness, hypertension and convulsion.

Physical monitoring: At hourly intervals undertake, blood pressure and heart rate monitoring

Medical/Emergency support: If post injection syndrome symptoms appear, contact medical staff immediately including dialling 999 if necessary. Additionally monitor BP, HR, Temp and Respiratory Rate.

Time	Observations	Nurse/HCA Signature
Date/Time of starting observation: Baseline BP _____ Baseline Heart Rate _____		
15 min post administration	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐	
30 min post administration	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐	
45 min post administration	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐	
60 min post administration	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐ Blood Pressure _____ Heart Rate _____	
1hr 30 min post administration	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐	
2hr post administration	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐ Blood Pressure _____ Heart Rate _____	
2hr 30 min post administration	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐	
Prior to leaving	No signs of weakness, dizziness, general malaise ☐ Alert ☐ Orientated ☐ No signs and symptoms of olanzapine overdose ☐ Blood Pressure _____ Heart Rate _____	
Monitoring End Time: ***Please scan completed monitoring form into PARIS***		