NHS Greater Glasgow & Clyde
Mental Health Services

Protocol for the use of Unlicensed Olanzapine Injection

Indication

Eli Lilly ceased marketing Olanzapine intramuscular injection (Zyprexa) in the UK for commercial reasons in 2013. The preparation retains marketing authorisation throughout the rest of the EU. Consequently, it has to be imported from Europe making the version used technically unlicensed in the UK.

The licensed indications for the original UK version of olanzapine injection still apply i.e. the rapid control of agitation and disturbed behaviour in patients with schizophrenia or in mania, when oral therapy is inappropriate[1] and it remains a treatment option within GG&C's Guideline for use of Intramuscular Medication for Acutely Disturbed Behaviour.[2]

PMG(MH) produced guidelines for the use of olanzapine injection in 2008.[3] This protocol replaces those guidelines.

Informed consent

As a treatment option for acutely disturbed behaviour, it is unlikely that prior consent for the use of intramuscular olanzapine could be obtained. In fact, it is the view of the Mental Welfare Commission for Scotland that individuals cannot give advance consent to the potential use of intramuscular medication.[4] Adherence to the principles contained in the Adults with Incapacity (Scotland) Act, 2000 and/or Mental Health (Care and Treatment) (Scotland) Act 2003 is mandatory in the case of intramuscular medication for acutely disturbed behaviour.

Due to its unlicensed status, explanation for the rationale of treatment choice should be given at a suitable time during the patient's treatment.[5] Patient information explaining unlicensed medication in general terms is available via the Choice and Medication portal, as is a specific olanzapine leaflet. [6]

Documentation

The consultant psychiatrist must make a clear record of the rationale for prescribing an unlicensed medication within the patient's case notes and document the discussion with the patient. Nursing staff in the ward must be informed of the medicine's unlicensed status and ward clinical pharmacists must ensure that staff are aware of the unlicensed status.

When ordering olanzapine intramuscular injection, the patient's initials and CHI should be included on the requisition as well as the phrase "as per protocol" for the order to be processed.

A record of administration of unlicensed medication must be kept (as per unlicensed medication policy).[7] This must include drug batch numbers, patient name and CHI number. The comments section of the recording sheet may be used for the purpose of documenting the batch number. It is the responsibility of the nurse in charge to ensure this occurs.

When supplying olanzapine intramuscular injection from pharmacy, pharmacy staff must ensure that batch numbers are documented on the requisition.

Review

It is recommended that this preparation only be prescribed in the once only section of the prescription sheet as it is not anticipated to be required on an on-going basis.

Monitoring

- Blood pressure (lying & standing)
- Pulse
- Respiration
- Temperature
- Level of hydration
- Level of consciousness

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At least hourly until the patient is ambulatory and there are no concerns about physical health. Monitor more regularly if the patient appears to be asleep or sedated, has taken illicit drugs or alcohol, has a pre-existing physical health problem or has experienced any harm as a result of any restrictive intervention. [2]

Dose range [1,8,9,10]

- **Adults:** 5 – 10mg by intramuscular injection. A repeat dose of 5 – 10mg may be given after a minimum of 2 hours. **Maximum daily dose** is 20mg (includes any oral olanzapine), with not more than 3 injections in 24 hours. Maximum treatment course is 3 days.

- **Elderly:** 2.5 – 5mg by intramuscular injection. A repeat dose of 2.5 – 5mg may be given after a minimum of 2 hours. **Maximum daily dose** is 20mg (includes any oral olanzapine), with not more than 3 injections in 24 hours. Maximum treatment course is 3 days

- **Adolescents:**[10] 2.5 - 5mg by intramuscular injection (depending on age, weight, previous exposure to antipsychotic medication, and whether has underlying neurodevelopmental disorder/LD). A repeat dose of 2.5 - 5mg may be given after a minimum of 2 hours. **Maximum daily dose** is 10mg - 20 mg (again dependent on above parameters and including any oral olanzapine), with not more than 3 injections in 24 hours. Maximum treatment course is 3 days.

Side effects

Common (<1/10 and >1/100)	sedation, altered heart rate (tachy and bradycardia), hypotension, postural hypotension, discomfort at the injection site
Uncommon (<1/100 and >1/1000)	reduced respiratory rate, abnormal heart rhythms

In addition, the injection shares side effects associated with oral olanzapine (see latest Summary of Product Characteristics for full details[11])

Contraindications

- Hypersensitivity to olanzapine or any other excipients in Zyprexa injection.
- Known narrow angle glaucoma

Cautions

- Unstable medical conditions e.g. acute MI, unstable angina, severe hypotension
- Concomitant use of benzodiazepines - **If the patient is considered to need parenteral benzodiazepine treatment, this should not be given until at least one hour after IM olanzapine administration. If the patient has received parenteral benzodiazepine, IM olanzapine administration should only be considered after careful evaluation of clinical status, and the patient should be closely monitored for excessive sedation and cardio-respiratory depression.**
- Hypotension
- Dementia related psychosis and/or behavioural disturbance
- Parkinson's disease
- Neuroleptic Malignant Syndrome
- Hyperglycaemia & diabetes
- Lipid alterations
- Prostatic hypertrophy
- Paralytic ileus
- Hepatic function
- Neutropenia

- Prolonged QT interval
- Thromboembolism
- Seizures
- Tardive dyskinesia
- Postural Hypotension
- Pregnancy

Interactions

- Caution should be exercised in patients who consume alcohol or take medicines that can induce hypotension, bradycardia, respiratory or CNS depression
- Benzodiazepines – see above
- CYP1A2 inducers e.g. smoking, carbamazepine. May lead to reduced olanzapine concentrations.
- CYP1A2 inhibitors e.g. fluvoxamine. May lead to increased olanzapine concentrations.
- Drugs known to prolong QT interval

References

1. Summary of Product Characteristics Zyprexa injection. Eli Lilly. Accessed via European Medicines Agency on 8/8/17 www.ema.europa.eu/ema

2. NHS GG&C Mental Health Services. Guideline for use of Intramuscular Medication for Acutely Disturbed Behaviour in Mental Health and Associated Services.MHS 40. April 2016

3. NHS GG&C. Prescribing Guidance. The use of Olanzapine IM. PMG(MH) 2008

4. Mental Welfare Commission for Scotland. Advice Notes. Medical Treatment under Part 16 of the Mental Health (Care and Treatment) (Scotland) Act 2003.

5. GMC Good practice in prescribing and managing medicines and devices. Updated Dec14 http://www.gmc-uk.org/guidance/ethical_guidance/14316.asp

6. Choice and Medication. Unlicensed medications handy fact sheet and olanzapine PIL http://www.choiceandmedication.org/nhs24/

7. NHS Greater Glasgow and Clyde Area Drug and Therapeutics Committee Policies Relating to the Management of Medicines Section 9.1 Acute Unlicensed Medicines Policy (ULM Policy)

8. Martindale. The Complete Drug Reference. https://www.medicinescomplete.com/mc/martindale/2009/ Accessed 8/8/17

9. Bazire S. Psychotropic Drug Directory 2018; Lloyd Reinhold Publications

10. Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry; 13th edition: Wiley Blackwell

11. Summary of Product Characteristics Zyprexa. Eli Lilly. http://www.medicines.org.uk/emc/medicine/614 Accessed 8/8/17