

WATAG Advisory Note:**Olanzapine Intramuscular Injection 10mg (Zyprexa®)**

Olanzapine IM injection is now available in Australia for the following TGA approved Indications:

- *“The rapid control of agitation and disturbed behaviours in patients with schizophrenia and related disorders and in patients with acute mania associated with bipolar disorder I when oral therapy is not appropriate”.*
- *“The rapid control of agitation and disturbed behaviours in patients with dementia when oral therapy is not appropriate”*

****Note that these are different registered indications from the oral formulation of olanzapine***

Olanzapine IM appears to demonstrate both efficacy and safety in clinical trials with fewer extrapyramidal side effects in comparison with haloperidol IM. However, it should be noted that clinical experience is limited and that trial subjects may not have been representative of severely agitated patients⁽¹⁻⁴⁾. Only one study supports the use of IM olanzapine in patients with dementia⁽⁴⁾ and there is accumulating evidence regarding the increased risk of stroke in the use of both risperidone and olanzapine for the treatment of behavioural disturbance with dementia⁽⁵⁾.

Recommendations for the use of Olanzapine IM:

- The therapeutic aim in acute agitation is sedation, and not antipsychotic effect. Benzodiazepines therefore remain the first option in the treatment of acute agitation, in accordance with the WATAG Antipsychotic Guidelines 2003
- Where treatment with an intramuscular antipsychotic is deemed necessary, olanzapine IM may be considered for the approved indications in the following circumstances:
 - **Antipsychotic-naïve patients,**
 - **Patients with a significant risk of experiencing extrapyramidal side-effects (EPSE).**
- The maximum dose should be 30mg/24hours (oral plus IM) and 10mg as a single IM administration.

- **In view of the risk of stroke/ cardio-vascular accidents (CVA), olanzapine IM should NOT be used in the treatment of acute agitation in the elderly.**
- An oral antipsychotic should be introduced at the first opportunity.
- Separate orders must be written for oral and IM doses. The option of combining oral and IM prescription should be avoided because of the high peak effects associated with intramuscular doses.
- **In view of the lack of evidence in severely agitated patients, current best practice requires careful patient monitoring for efficacy and adverse effects, and for this information to be documented in the patient's case notes.**

See Clinical Trial Summary- Appendix A

APPENDIX A

◆ Clinical Trial Summary- Olanzapine IM

- ◆ There are four main trials to support the efficacy of intramuscular olanzapine in the rapid control of agitation and disturbed behaviours. Two trials were conducted in patients with schizophrenia (SCZ), schizoaffective or schizophreniform disorder (N=270 ⁽¹⁾ & 311 ⁽²⁾), one in patients with bipolar mania (N=201 ⁽³⁾) and one in patients with dementia (N=272 ⁽⁴⁾).
- ◆ All trials were for the duration of 24hours, during which time patients could receive up to three injections (second injection had to be at least 2 hours after first injection, when the primary efficacy measure was assessed).
- ◆ All trials were placebo controlled and involved the use of the comparator haloperidol (two schizophrenia trials) or lorazepam (dementia and bipolar mania trials).
- ◆ In general, faster onset shown with olanzapine compared with haloperidol (30mins to be superior to placebo compared with 60mins in one SCZ trial⁽¹⁾ and 15mins compared with 30mins in another study⁽²⁾). Faster onset compared to lorazepam in bipolar mania trial and in dementia trial (30mins compared with 60mins in latter). Hypotension with olanzapine does not seem to have been a significant adverse event observed in trials, even in the elderly dementia trial in which many patients had cardiac comorbidity⁽⁴⁾. No acute dystonias seen in olanzapine treated patients compared with several on haloperidol ^(1,2,3). Olanzapine has similar effect to placebo on QTc interval – trials also confirmed safety of haloperidol IM in this respect too.
- ◆ Olanzapine IM was not shown to be more benzodiazepine-sparing than haloperidol in trials ^(1,2).
- ◆ All patients were deemed sufficiently agitated to be given parenteral treatment. **However, they were not so agitated that they were unable to give written, informed consent.**

References:

- Breier A et al. A double-blind placebo-controlled dose-response comparison of intramuscular olanzapine and haloperidol in the treatment of acute agitation in schizophrenia. *Arch Gen Psych* 2002; 59:441-8
 - Wright P et al. A double blind, placebo-controlled comparison of intramuscular olanzapine and intramuscular haloperidol in the treatment of acute agitation in schizophrenia. *Am J Psychiatry* 2001;158: 1149-51
 - Meehan K et al. A double-blind, randomised comparison of the efficacy and safety of intramuscular injections of olanzapine, lorazepam or placebo in treating acutely agitated patients diagnosed with bipolar mania. *J Clin Psychopharmacol* 2001; 21: 389-397
 - Comparison of rapidly acting intramuscular olanzapine, lorazepam and placebo: a double-blind, randomised study in acutely agitated patients with dementia.
5. Committee on Safety of Medicines. March 2004