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Schizophrenia and related psychoses CHAPTER 1 understanding of these factors might allow for possible barriers to the optimal implementation of this treatment to be identified.^{24–26} A study in the USA found that patients with first-episode schizophrenia were largely willing to accept long-acting treatment.²⁷ This suggests that the relatively low usage of LAIs in the USA might be partly a result of reluctance on the part of clinicians, rather than resistance from patients.^{28,29}

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- **Test doses** Because of its long half-life, any adverse effects that result from the administration of LAI antipsychotic medication are likely to be long lived. Therefore, such treatment should be avoided in patients with a history of serious adverse effects that would warrant immediate discontinuation of the medication, such as neuroleptic malignant syndrome (NMS). For LAI FGAs, a test dose, consisting of a small dose of active drug in a small volume of oil, serves a dual purpose: it is a test of the patient's sensitivity to EPS and of any sensitivity to the base oil. For LAI SGAs, test doses may not be required (there is a lower propensity to cause EPS and the aqueous base is not known to be allergenic), although they could be considered appropriate where a patient is suspected of being non-adherent to oral antipsychotic medication and the LAI preparation will be the first exposure to guaranteed antipsychotic medication delivery. For both LAI FGAs and SGAs, prior treatment with the equivalent oral formulation, establishing the optimally effective and tolerated dose, is advised,³⁰ but may not be necessary from a pharmacokinetic viewpoint. Most LAI SGAs can be used as sole treatment from the outset, although loading doses are usually necessary (e.g. for paliperidone and aripiprazole).
- **Begin with the lowest therapeutic dose** For LAI FGA medications, there is limited evidence for a clear dose-response effect and a near absence of data on optimal dosing. However, low doses (within the licensed range) may be at least as effective as higher ones.^{31–34} For the LAI antipsychotic medications that are commonly used, it remains uncertain that the dosages and frequency of injections achieve the optimal benefit-risk balance.^{35–37}
- **Administer at the longest possible licensed interval** All LAI antipsychotic medications can be safely administered at their licensed dosing intervals, bearing in mind the maximum recommended single dose. There is no evidence to suggest that shortening the dose interval improves efficacy. Moreover, less frequent administration may be desirable, as the IM injection site can be a cause of discomfort and pain; these reactions may be more common with LAIs that have oil-based formulations.^{38,39} Although there are reports of illness deterioration in some patients in the days before their next injection is due, plasma drug concentrations may continue to fall for some hours (or even days with some preparations) after each injection. In this context, a patient's apparent recovery soon after the injection makes little

sense. More importantly, at steady state, trough plasma levels (immediately before and after the dose) are usually substantially above the threshold concentration required for therapeutic effect.^{30,40,41}

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