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Conclusion

306 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 2 neither decreases nor increases the risk of depressive relapse. Risperidone LAI may be less effective than oral olanzapine. It might be assumed that paliperidone LAI has similar effects to risperidone LAI. Oral paliperidone prevents manic relapse in bipolar disorder,¹⁸ there are a few supportive mirror-image studies^{6,7} and case reports describe good outcomes with the LAI form.^{19,20} Aripiprazole LAI protects against manic relapse but does not appear to affect risk of depression. Data for FGAs in bipolar disorder are scarce and generally of low quality (open trials, case series and retrospective analyses). In these studies, FGA LAIs seem to reduce the risk of relapse compared with prior treatments. The largest (open) study¹² (n = 85) suggested flupentixol decanoate (20mg every 2–3 weeks) reduced the risk of elevated mood episodes. Reports describe similar effects for other FGA LAIs. The one RCT conducted with flupentixol LAI¹² showed no effect and no superiority over lithium. Considering this single RCT and all of the small and uncontrolled observations, there is very little evidence to support the often-repeated lore that flupentixol LAI increases the risk of manic relapse and haloperidol LAI and fluphenazine LAI increase the risk of depressive relapse (or that FGAs provoke depression). It is notable that authors of systematic reviews^{21,22} reiterate this view, which seems to be based on solely the observed increase in depressive episodes in the open study conducted by Ahlfors and colleagues.¹² In fact, this increase occurred only in subjects whose lithium treatment had been stopped immediately before the study began. Nonetheless, oral haloperidol, when used for mania, is more likely than oral SGAs to cause a switch to depression²³ so some caution is clearly required. There are no controlled comparisons of FGA and SGA LAIs.^{1–3} A Taiwanese retrospective cohort study²⁴ reported a higher risk of depressive episode recurrence and a higher likelihood of hospitalisation in those prescribed FGA LAIs (50% were prescribed flupentixol, 25% haloperidol and 25% other drugs) compared with those prescribed risperidone LAI. Of particular note was the substantial rate of treatment discontinuation. At 1 year only 7.2% of those initially prescribed risperidone and 2.2% of those initiated on FGA LAIs remained on the original treatment. Another observational study found both SGA and FGA LAIs to be effective but only when treatment continued for at least 6 months.²⁵

Conclusion

- ■ Support for the use of FGA LAIs in bipolar disorder is weak.
- ■ Very limited evidence suggests FGA LAIs may be effective in reducing recurrence of mania/hypomania but they do not prevent recurrence of depression and may increase the risk.
- ■ Risperidone LAI and aripiprazole LAI are robustly associated with a reduced risk of recurrence of episodes of mania/hypomania compared with placebo.
- ■ Risperidone LAI and aripiprazole LAI have no effect on the risk of depressive recurrence.
- ■ There is limited evidence to support the benefit of LAIs over oral antipsychotic treatment in bipolar maintenance.
- ■ As with other conditions, the use of LAIs offers the advantage of transparency in respect to compliance: the LAI injection is either given or it is not.

Revision #1

Created 2026-01-04 20:14:27 UTC by Omar Ayman

Updated 2026-01-04 20:14:27 UTC by Omar Ayman