

80 - Two injection start

Two-injection start

Schizophrenia and related psychoses CHAPTER 1 Aripiprazole long-acting injection Aripiprazole 1--monthly Aripiprazole lacks the prolactin-related and metabolic adverse effects of other SGA LAIs and so is a useful alternative to them. Placebo-controlled studies show a good acute and longer-term effect in the treatment of schizophrenia.¹ In the USA, aripiprazole long-acting injection (ALAI) is approved for maintenance monotherapy in bipolar I disorder in adults.² In the UK and some other countries, the use of aripiprazole LAI in bipolar is off-label. Oral aripiprazole 10–20mg/day should be given for 14 days to establish tolerability and response. This oral run-in is also a vital part of the loading process.³ In patients switching from another oral antipsychotic to ALAI, aripiprazole should have been effective and tolerated in the past. The current antipsychotic should be continued for the first 14 days following the initial ALAI administration.² One of the following two regimens may be followed for administering the starting dose of aripiprazole LAI.⁴

One-injection start On the day of initiation, administer one injection of 400mg aripiprazole LAI and continue treatment with 10–20mg/day oral aripiprazole for 14 consecutive days (i.e. 28 days in total) to maintain therapeutic aripiprazole concentrations during initiation. In the absence of the 14-day oral overlap, plasma levels may not be sufficient to afford a therapeutic effect.³

Two-injection start On the day of initiation, administer two separate injections of 400mg aripiprazole LAI at separate injection sites in two different muscles (separate gluteal, separate deltoid or gluteal and deltoid injection sites), together with one 20mg dose of oral aripiprazole. Oral therapy should not continue after this point. The necessity for the single oral dose is doubtful, given it represents only 2.5% of the total dose given. One month after the day of initiation, begin a regimen of 400mg each month (the manufacturer appears to define 'monthly' as every 28 days).⁴ A monthly dose of 400mg aripiprazole is equivalent to 15–20mg of daily aripiprazole.⁵ After the one-injection plus oral starting regimen, peak plasma levels are reached 7 days post-injection, with trough levels occurring at 4 weeks.⁶ After two-injection start, peak plasma concentration is observed at 5–7 days when administered in the gluteal muscle and at 4 days for the deltoid muscle.⁷ Steady-state plasma levels are achieved after the fourth IM injection for both administration sites (see Table 1.10 for missed doses).⁷ A lower dose of 300mg a month can be used in those not tolerating 400mg or for those who are poor metabolisers via CYP2D6. A dose of 200mg/month may only be used for those patients receiving particular enzyme-inhibiting drugs. Most common adverse events are increased weight, akathisia, insomnia and injection site pain.^{4,7}

86 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 While there are no official guidelines for switching to aripiprazole, the recommendations in Table 1.11 are based on our interpretation of existing pharmacokinetic data. Table 1.10 Delayed doses of aripiprazole long-acting injection.⁴ ALAI dose missed Regimen 2nd or 3rd ALAI dose is missed and time since last

injection is >4 weeks and <5 weeks Administer as soon as possible 2nd or 3rd ALAI is missed and time since last injection is >5 weeks Give oral aripiprazole for 14 days and one dose of ALAI or Give two ALAI injections at different sites + single dose 20mg aripiprazole If \geq 4th ALAI is missed and time since last injection is >4 weeks and <6 weeks Administer as soon as possible If \geq 4th ALAI is missed and time since last injection is >6 weeks Give oral aripiprazole for 14 days and one dose of ALAI or Give two ALAI injections at different sites + single dose 20mg aripiprazole ALAI, aripiprazole long-acting injection. Table 1.11 Switching to 1-monthly aripiprazole long-acting injection.

Switching from Aripiprazole LAI regimen Oral antipsychotics Cross-taper antipsychotic with oral aripiprazole* over 2 weeks One-injection start Start aripiprazole LAI, continue aripiprazole oral for another 2 weeks then stop Two-injection start Start aripiprazole LAI as indicated above after 2 weeks of oral aripiprazole, then stop oral treatment** Depot antipsychotics (not Risperidone Consta) Start oral aripiprazole* on day the last depot injection was due One-injection start Start aripiprazole LAI after 2 weeks then stop oral aripiprazole 2 weeks later Two-injection start Start aripiprazole LAI as indicated above after 2 weeks of oral aripiprazole, then stop oral treatment** Risperidone Consta Start oral aripiprazole* 4–5 weeks after the last risperidone injection One--injection start Start aripiprazole LAI 2 weeks later; discontinue oral aripiprazole 2 weeks after that Two-injection start Start aripiprazole LAI as indicated above after 2 weeks of oral aripiprazole, then stop oral treatment** * If prior response and tolerability to aripiprazole are known, pre-injection oral aripiprazole may not be strictly required. However, attainment of effective aripiprazole plasma levels is dependent upon 4 weeks of oral supplementation for the one-injection start regimen. Similarly, for the two-injection start regimen, the pharmacokinetic modelling study was based on plasma levels from oral aripiprazole being at (therapeutic) steady state on the day of initiation. It may be sufficient to start aripiprazole LAI in the absence of prior oral aripiprazole where the prior antipsychotic is at a therapeutic level. Continuation for 14 days is presumably also required. ** If oral aripiprazole cannot be given at all (e.g. patient refusal) always use the two-injection starting regimen. This 800mg dose is likely to afford sustained therapeutic plasma concentrations even in the absence of prior oral treatment. LAI, long-acting injection.

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