

90 - Paliperidone long acting injection 1 monthly

Paliperidone long-acting injection 1-monthly

Schizophrenia and related psychoses CHAPTER 1 Paliperidone palmitate long-acting injection Paliperidone (9-hydroxyrisperidone) is the major active metabolite of risperidone. Paliperidone palmitate is the ester prodrug of paliperidone. It is available as a monthly, 3-monthly and 6-monthly LAI. The ester is an aqueous nanosuspension, which is hydrolysed to paliperidone after IM administration and slowly absorbed into the circulatory system.^{1,2} Paliperidone long-acting injection 1-monthly After the recommended initial loading dose of paliperidone LAI 1-monthly (PP1M), active paliperidone plasma levels are seen within a few days, so co-administration of oral paliperidone or risperidone during initiation is not required from a pharmacokinetic viewpoint but some patients may benefit from gradual withdrawal.³ Dosing consists of two initiation doses (deltoid) followed by monthly maintenance doses (deltoid or gluteal). Administering a single IM dose to the deltoid muscle results in an average 28% higher peak concentration compared with IM injection to the gluteal muscle.³ Therefore, the two deltoid muscle injections on days 1 and 8 help to attain therapeutic drug concentration quickly. Improvement in psychotic symptoms has been observed as early as day 4.³ Table 1.17 gives information on dose and administration of PP1M. Table 1.19, later in this section, provides guidance on how to switch to PP1M.³ The second initiation dose may be given 4 days before or after day 8 (after the first initiation dose on day 1).³ The manufacturer recommends that patients may be given maintenance doses up to 7 days before or after the monthly time point.³ This flexibility should help to minimise the number of missed doses. See the manufacturer's information for full recommendations regarding missed doses.³ Points to note ■ ■ No test dose is necessary for paliperidone palmitate. However, patients should ideally be stabilised on or have previously responded to oral paliperidone or risperidone. ■ ■ After a single IM injection, paliperidone is continuously released into the systemic circulation from day 1 for at least 4 months.³ Table 1.17 Paliperidone dose and administration information.³ Dose Route Initiation Day 1 150mg IM Deltoid only Day 8 (±4 days) 100mg IM Deltoid only Maintenance Every month (±7 days) thereafter 50-150mg IM* Deltoid or gluteal** * The maintenance dose is perhaps best judged by consideration of what might be a suitable dose of oral risperidone and then giving paliperidone palmitate in an equivalent dose (Table 1.18). Pre-treatment with oral risperidone is helpful in establishing efficacy and tolerability of a given dose. ** Continuation with deltoid

injections for the first 6 months may be considered in some patients who switch from higher doses of oral paliperidone or risperidone.³

94 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 ■ ■ The median time to maximum plasma concentration is 13 days,³ and half-life ranges from 25 to 49 days. ■ ■ Patients receiving fewer than 12 injections a year have an increased risk of relapse – correct dosing is critical to the effectiveness of paliperidone monthly.^{4,5} Paliperidone LAI has been compared with haloperidol depot given in a loading dose schedule matching that of paliperidone.⁹ The two formulations were equally effective in preventing relapse but paliperidone increased prolactin to a greater extent and caused more weight gain. Haloperidol caused more akathisia and more acute movement disorder, and there was a trend for a higher incidence of tardive dyskinesia. The average dose of haloperidol was around 75mg a month, a dose rarely used in practice. There are two studies comparing monthly paliperidone LAI with aripiprazole LAI. The first was a 28-week randomised head-to-head trial that found aripiprazole monthly injection superior in the improvement of quality of life and functioning in the short term, although the aripiprazole group included more younger patients.¹⁰ The second study compared the two LAIs in patients with psychosis and comorbid substance use disorder. Improvement in quality of life and reduced substance cravings were seen with both LAIs, although aripiprazole fared better. Overall, there was no clear clinically meaningful superiority for aripiprazole over paliperidone in either of these studies.¹¹ Table 1.18 Approximate dose equivalence for paliperidone and risperidone.^{3,6}

Risperidone oral (mg/day) (bioavailability = 70%) ⁷	Paliperidone oral (mg/day) (bioavailability = 28%) ⁸	Risperidone LAI (Consta) (mg/2 weeks)	Paliperidone palmitate (mg/monthly) (bioavailability = 100%) ³
3	3	50	6
6	37.5	4	50
6	4	50	6

– Table 1.19 Switching to paliperidone palmitate 1-monthly.³

Switching from Recommended method of switching Comments No treatment Give the two initiation doses: 150mg IM deltoid on day 1 and 100mg IM deltoid on day 8 The manufacturer recommends a dose of 75mg monthly for the general adult population.¹² This is approximately equivalent to 3mg/day oral risperidone (Table 1.18). In practice, the modal dose is 100mg/month.¹³ Maintenance dose starts 1 month later Maintenance dose adjustments should be made monthly. However, the full effect of the dose adjustment may not be apparent for several months.³ Oral paliperidone/ risperidone Give the two initiation doses followed by the maintenance dose (see Table 1.18 and prescribe equivalent dose) Oral paliperidone/risperidone can be discontinued at the time of initiation; some patients may benefit from a gradual withdrawal (Continued)

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