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subcutaneous long acting injection

Risperidone subcutaneous long-acting injections

Schizophrenia and related psychoses CHAPTER 1 Risperidone ISM® (Risvan, Okedi) Risperidone ISM is an injectable suspension of risperidone suitable for stable patients who have previously responded and tolerated risperidone.⁷ Risperidone ISM employs in situ microparticle technology (ISM) to provide effective plasma levels as early as 2 hours following IM administration without requiring a loading dose or oral supplementation. An initial peak in plasma concentration is seen within 24–48 hours of administration with a second peak appearing between days 18 and 25. The delayed appearance of the second peak should be noted when assessing clinical efficacy, tolerability and when making changes to dose.⁷ The dosing interval for the injection is every 28 days (Table 1.24). Risperidone ISM is effective both as an acute⁹ and maintenance¹⁰ treatment and is generally well tolerated, although increased prolactin is common, as with all risperidone formulations.⁹ An indirect comparison with other SGA LAIs suggested somewhat better tolerability for risperidone ISM, but this study was authored by researchers linked to risperidone ISM's manufacturers.¹¹ Its main advantages are the absence of a loading dose requirement and the 28-day administration interval. The main disadvantages of risperidone ISM are that it is not suitable for patients requiring 2mg or 6mg/day of oral risperidone and that it may not be given to patients with a creatinine clearance of less than 60mL/minute. Risperidone subcutaneous long-acting injections Perseris® RBP-7000 (Perseris) is SC risperidone LAI that is available in 90mg and 120mg dosage forms. It is given every 28 days. The lower dose is equivalent to 3mg/day oral risperidone and the higher dose 4mg/day.¹² There are no specific formulations corresponding to 2mg or 6mg/day of oral risperidone. However, two SC injections of 90mg RBP-7000 can be given to afford a similar plasma concentration to 6mg oral risperidone.¹³ Table 1.24 Initiation of risperidone ISM. Dose Route Initiation Day 1* 75mg or 100mg IM Deltoid or gluteal Maintenance Every 28 days (±3 days) thereafter 75mg IM or 100mg** IM Deltoid or gluteal * No loading dose is required but response and tolerability to oral risperidone must be assured by prior oral supplementation for at least

14 days. ** 75mg risperidone ISM is recommended as maintenance treatment by the manufacturer. It seems likely that 100mg will be required by most people (equivalent to 4mg/day oral risperidone).

102 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 RBP-7000 is suitable for SC administration in the abdominal region or back of the upper arm.¹⁴ It has a biphasic release pattern, with the first peak occurring 4–6 hours after administration and the second at 10–14 days post-dose.¹⁵ The active metabolite, paliperidone, has its first peak at 4–48 hours post-injection and the second at 7–11 days. Steady state is achieved after the second SC injection.¹⁶ The injection is acutely effective at both licensed doses (although 120mg may be better than 90mg), without the need for oral pre-treatment or oral supplementation, although tolerability with oral risperidone should be established before commencing treatment.^{17,18} In the longer term, monthly doses of 120mg are effective in maintaining response.^{19,20} RBP-7000 is rapidly active, achieving therapeutic plasma concentration on the first day.²¹ Disadvantages include the need for refrigerated storage and a complex multi-step injection procedure. The complexity of preparation and subcutaneous administration are new to psychiatry and failure to follow the instructions might result in dosage errors.^{14,21,22} RBP-7000 appears to be well tolerated and has a safety profile similar to that of oral risperidone. In clinical trials, the most commonly reported adverse effects were injection site pain and weight gain.^{16,19} See manufacturer’s advice on how to initiate RBP-7000.²¹ Uzedy® (TV-46000) Uzedy is a risperidone extended-release injectable suspension licensed for SC administration in the abdominal region or upper arm. It is available as a 1- or 2-monthly injection (see Table 1.25 for equivalent doses).²³ Uzedy does not require oral supplementation or loading doses but response and tolerability to oral risperidone should be established before initiating treatment. The pre-filled syringe must be stored in the fridge and allowed to sit at room temperature for at least 30 minutes before administration. The syringe content is solid at refrigerated temperatures and converts to liquid at 20–25°C. Steady-state plasma level of Uzedy is reached after two SC injections. Therapeutic concentrations are seen on day one. Like other risperidone injections, Uzedy has a biphasic release pattern with two peak levels. In clinical trials,^{24–26} Uzedy was effective both acutely and as relapse prevention. One-monthly administration afforded numerically better protection against relapse than two-monthly injections.²⁷ The most commonly reported adverse effects were injection site pain, injection site nodules, weight gain and EPSEs. Most participants had an F20 diagnosis for 20 years and were stabilised on oral risperidone for at least 12 weeks before trial entry.

Table 1.25 Equivalent doses – risperidone-based long-acting injections.^{6,7,28–33} Risperidone oral (mg/day) (bioavailability = 70%) Paliperidone oral (mg/day) (bioavailability = 28%) Risperidone LAI RBP-7000* (mg/28 days) Uzedy* (mg/ monthly) Uzedy* (mg/2 monthly) Paliperidone palmitate** (mg/monthly) Paliperidone palmitate** (mg/3-monthly) (Consta)* (mg/2weeks) Rykindo* (mg/2 weeks) Risperidone ISM~† (mg/28 days) – – 12.5*** – – – – – 3 25 – – 100 175 6 37.5 37.5 90 150 263 9 50 120 200 350 12 – – – –†† 250 525 * Bioavailability assumed to be 100%. ** Bioavailability has been confirmed to be 100%. ~ Initiate risperidone ISM 24 hours after the last oral dose of risperidone. † Recommended starting dose for patients with renal or hepatic impairment⁸ or poor antipsychotic tolerability, not studied in clinical trials.³⁴ †† 180mg (two SC injections of 90mg) of RBP-7000 is equivalent to 6mg daily risperidone dose.

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