Antipsychotic treatment of schizophrenia and schizophrenia-like illnesses is associated with reduced psychotic symptoms, an increased time to recurrence of psychotic symptoms, and reduced rates of hospital admissions. However, people diagnosed with schizophrenia often do not fully adhere to oral medication regimens. In an effort to improve adherence, physicians often recommend long-acting intramuscular antipsychotic injections. Pharmaceutical manufacturers typically prepare long-acting intramuscular formulations of antipsychotics as esters, suspended in oil. These formulations are absorbed and eliminated by the body at a slower rate than oral preparations. When it produced the long-acting formulation of risperidone, the manufacturer did not esterify the drug. They instead produced an aqueous suspension of risperidone microspheres. As a result, long-acting injections of risperidone must be refrigerated, reconstituted with a diluent supplied by the manufacturer, and administered within 6 hours of reconstitution. In addition, clinicians need to administer the risperidone long-acting formulation bi-weekly to maintain a therapeutic concentration.

**Paliperidone**

Paliperidone is the active metabolite of risperidone. Cytochrome P450 enzymes 2D6 and 3A4 metabolise risperidone to 9-hydroxyrisperidone, marketed orally as paliperidone. We previously reviewed its efficacy and safety for the Cochrane Collaboration. To make a long-acting injectable formulation of paliperidone, its hydroxyl group is esterified. Paliperidone palmitate is an aqueous suspension with low water solubility that is absorbed and eliminated slowly. It is supplied in pre-filled syringes of 39, 78, 117, 156 or 234 mg. Clinicians reconstitute it with vigorous shaking before administration. Paliperidone palmitate does not require refrigeration and can be administered monthly. After intramuscular administration, the drug slowly dissolves. After hydrolysis to paliperidone, it becomes available in the systemic circulation. The drug is measured in plasma as early as the first day of administration and lasts as long as 126 days, reaching maximum plasma concentration at 13 days. We have previously reviewed its efficacy and safety for the Cochrane Collaboration.

**Method**

**Search methods**

We searched the Cochrane Schizophrenia Group Specialised Register for randomised controlled trials (RCTs) comparing paliperidone palmitate with any other treatment for schizophrenia. We inspected references of identified studies.
Paliperidone palmitate v. depot risperidone

Two additional studies\(^4,15\) compared paliperidone palmitate with depot risperidone (\(n=1969\)). In these flexibly dosed trials, the mean doses of paliperidone palmitate were 73.3 mg and 104.6 mg every 4 weeks compared with depot risperidone at mean doses of 35.3 mg and 31.7 mg every 2 weeks. There was no difference for leaving these studies early for any reason between paliperidone palmitate and depot risperidone (\(n=1969\), 2 RCTs: RR = 1.12, 95% CI 1.00–1.25). Those receiving paliperidone palmitate were no more likely to have a recurrence of psychotic symptoms (\(n=1961\), 2 RCTs: RR = 1.23, 95% CI 0.98–1.53). There were a total of six deaths in these two trials, with five in the paliperidone palmitate groups. Although this difference was not significant (\(n=1967\), 2 RCTs: RR = 3.62, 95% CI 0.60–21.89), the small number of these events and wide confidence interval makes it unclear whether this finding is meaningful. Patients randomised to paliperidone palmitate were significantly less likely to use anticholinergic medications (\(n=1587\), 2 RCTs: RR = 0.67, 95% CI 0.55–0.82; NNB 13, 95% CI 10–24).

We found no data regarding service use, quality of life, patient satisfaction or cost. Similarly, we found no randomised studies that compared paliperidone palmitate with any other treatments for schizophrenia or schizophrenia-like illnesses.

**Discussion**

In short-term studies, paliperidone palmitate is an efficacious antipsychotic drug. Its adverse effects are similar to oral paliperidone, oral risperidone and depot risperidone. Extrapyramidal side-effects, weight gain and tachycardia are more common with paliperidone palmitate than placebo. Paliperidone palmitate is associated with substantial increases in serum prolactin. Used at mean doses of approximately 70–110 mg every 4 weeks, it appears comparable in efficacy and tolerability with depot risperidone used at mean doses of approximately 35 mg every 2 weeks.\(^6,16\) People who received paliperidone palmitate were significantly less likely to receive anticholinergic medications. Paliperidone palmitate has two practical advantages over depot risperidone in that it does not need to be refrigerated and can be administered monthly rather than bi-weekly, but we found no clear benefit of paliperidone palmitate over depot risperidone.

This study confirms our suspicion that paliperidone palmitate will affect people with schizophrenia similarly to depot risperidone. For individual clinicians to select paliperidone palmitate over other long-acting injectable antipsychotics on the basis of appropriate evidence, researchers will need to conduct longer-term pragmatic studies that more closely resemble the lived experience of patients with schizophrenia. Appropriate comparators include fluphenazine decanoate, haloperidol decanoate, depot olanzapine and depot risperidone. Clinicians would also benefit from studies that assess the efficacy, adverse effects and safety of long-term use of paliperidone palmitate, including behaviour, mortality, satisfaction with treatment and cost-effectiveness in comparison with oral antipsychotics.

**Acknowledgements**

We thank our respective departments and the Cochrane Schizophrenia Group for their support. See also Nussbaum & Stroup.\(^9\)

**About the authors**

Abraham M. Nussbaum, Director, Adult Inpatient Psychiatry, Behavioral Health Service, Denver Health, Denver, and University of Colorado, USA.

T. Scott Stroup, Director, Program for Intervention Effectiveness Research, New York State Psychiatric Institute, and Columbia University, New York, USA.
References

Drug information update: paliperidone palmitate for schizophrenia
Abraham M. Nussbaum and T. Scott Stroup
The Psychiatrist Online 2013, 37:164-166.
Access the most recent version at DOI: 10.1192/pb.bp.113.042739

References
This article cites 11 articles, 0 of which you can access for free at: http://pb.rcpsych.org/content/37/5/164#BIBL

Reprints/permissions
To obtain reprints or permission to reproduce material from this paper, please write to permissions@rcpsych.ac.uk

You can respond to this article at /letters/submit/pbrcpsych;37/5/164

Downloaded from http://pb.rcpsych.org/ on September 27, 2017
Published by The Royal College of Psychiatrists

To subscribe to BJPsych Bulletin go to: http://pb.rcpsych.org/site/subscriptions/