Haloperidol decanoate long-acting injection (HDLAI): Results of a 1-year mirror-image study

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Abstract
Background: We sought to determine clinical outcomes of the prescribing of haloperidol decanoate long-acting injection (HDLAI) at 1 year.

Method: A 1-year mirror-image study of 84 inpatients initiated on HDLAI. Admissions and bed days in the year preceding HDLAI were compared with the year after initiation. Predictors for discontinuation were evaluated.

Results: At 1 year, 33% of patients remained on treatment. Patients starting HDLAI because of nonadherence were more likely to stop treatment [relative risk (RR) 1.72; 95% confidence interval (CI) 1.01, 2.91; \( p = 0.044 \)] whilst patients with a longer duration of illness were more likely to remain on treatment (RR 0.88; 95% CI 0.78, 1.00; \( p = 0.050 \)). In the bed days cohort overall, \( n = 65 \), there was a significant reduction in mean hospital admissions (1.4/patient/year to 0.6/patient/year; \( p = 0.0001 \)) but not bed days (55.6/patient to 45.0/patient; \( p = 0.07 \)) in the year following HDLAI initiation compared with the year before. Continuers had a significant reduction in mean bed days (53.1 to 4.0; \( p = 0.0002 \)) and hospital admissions (1.5 to 0.2; \( p = 0.0001 \)). Discontinuers demonstrated a significant reduction in hospital admissions (1.5 to 0.8; \( p = 0.0001 \)) but not bed days (56.7 to 64.5; \( p = 0.83 \)).

Conclusion: HDLAI was associated with a high treatment discontinuation rate. Hospital admissions fell in the year after HDLAI but there was no change in bed days. Our study suggests that patients with a longer duration of illness and patients initiated on HDLAI for reasons other than poor adherence may benefit from HDLAI initiation.

Keywords: antipsychotic, depot, haloperidol, hospital admission

Introduction
In 2014, McEvoy and colleagues reported results of the first double-blind comparison between a first- and second-generation long-acting injection.\(^1\) The study, comparing paliperidone palmitate (PPLAI) and haloperidol decanoate (HDLAI), found no overall difference in efficacy between the two treatments. Haloperidol in this study was used in strict accordance with a prescribed loading regimen and maintenance doses were lower than traditionally seen in practice. The incidence of specific adverse effects varied between the drugs, however, overall tolerability of both was broadly comparable: paliperidone was associated with more weight gain and higher serum prolactin levels and haloperidol was associated with more akathisia and the use of anticholinergic medication.

Separately, observational data for PPLAI from our own unit showed a reduction in both the number of hospital admissions and inpatient bed days in the 2 years after discharge compared with the 2 years before paliperidone initiation.\(^2\) At 1 year, 65% of patients remained on the PPLAI.\(^3\)

PPLAI is considerably more expensive than HDLAI. Based on the findings by McEvoy and co-workers that HDLAI is as effective and well...
tolerated as PPLAI, we changed our trust prescribing guidelines to include the recommendation that HDLAI be considered the long-acting injection of choice.

In this paper, we report the discontinuation rate, hospital bed days and admissions at 1 year for inpatients who started HDLAI between June 2014 and June 2015 in the South London and Maudsley NHS Foundation Trust.

Materials and method
All inpatients starting HDLAI between July 2014 and July 2015 were identified and followed for 1 year. HDLAI is supplied for inpatients from the trust pharmacy on submission of a valid prescription. Inpatients starting HDLAI were identified from these prescriptions. Demographic data and medication details were recorded from patients’ electronic medical notes, pharmacy notes and prescription charts. Medication details included the recorded reason for initiation of HDLAI, antipsychotic prescribed immediately before HDLAI and immediately after in those who stopped, reason for stopping treatment, reported adverse effects and a history of previous clozapine or HDLAI treatment. Initiation and maintenance doses and the haloperidol initiation regimen were recorded from the prescription. Patient data once collected were anonymised and stored in a secure database.

Ethics approval was not sought for the purpose of this study. The study was approved by the trust’s Drug and Therapeutics Committee, the locally designated approval committee. Our standard method had previously been assessed by our local ethical committee as not requiring ethical committee approval because treatment was not affected by our method and because data were anonymised. The decision to initiate HDLAI was an independent prescribing decision; this study did not influence clinical practice. Patient-identifiable data accessed for the purpose of data collection are readily available to clinicians involved in the study as part of their normal working practice. Patients were not required to give informed consent to the study.

Primary analysis
Our primary outcome was discontinuation with treatment at 1 year.

Secondary analyses
Change in admissions and bed days following treatment with HDLAI. We used a mirror-image study design to compare the number of hospital admissions and occupied hospital bed days before and after HDLAI initiation. The mirror was placed in three different places as previously described. In our main analysis, we compared the number of admissions and bed days in the year before haloperidol initiation with the year after discharge from the admission during which haloperidol was initiated (index admission), thus including the index admission only until HDLAI initiation and disregarding the remainder of the admission (see Figure 1).

Sensitivity analyses
We conducted two sensitivity analyses: In the first, the ‘mirror’ was placed at the point of initiation of haloperidol, including the entire index admission. In the second, the entire index admission was disregarded and the mirror placed at both the point of admission to and discharge from the index admission (see Figure 1).
Patients on forensic inpatient units were excluded from the analyses of admissions and bed days because their hospital stay is determined by the Ministry of Justice and may be independent of their clinical presentation.

**Statistical analysis**

All analyses were performed using STATA version 11.2 (StataCorp LP, College Station, Texas, USA).

**Treatment discontinuation**

Time to discontinuation of HDLAI was the outcome of interest. Patients were followed up for 365 days from the date of initiation of HDLAI until they discontinued treatment or dropped out of the study. Patients were regarded as discontinuers if they switched to another antipsychotic, stopped HDLAI or if the next HDLAI dose was not administered within 8 weeks of the last dose. Patients were regarded as continuers if they received uninterrupted treatment with HDLAI until the end of the follow-up period. We defined censoring as absence of the event at time of death or loss to follow up before the end of the study period. Patient baseline demographics at the time of initiation were summarized using descriptive statistics. Time to discontinuation was modelled using a multivariate Cox regression model. We first screened baseline variables (age, sex, ethnicity, diagnosis, duration of illness, treatment responsiveness, previous use of HDLAI, initiation regimen and reasons for initiating treatment) using a univariate Cox regression model and variables showing a significant association ($p < 0.2$) were included in the multivariate model. Categorical variables with multiple levels were collapsed prior to the regression analyses in order to avoid cells with sparse data. Continuous variables were assessed for linearity using Martingale residual plots and transformed using fractional polynomials. The proportional hazard assumption for each variable was tested using Schoenfeld residuals by time plots. Goodness of fit was assessed by Cox–Snell residual plots.

**Hospital admissions and bed days**

We expected hospital admissions and bed days to be non-normally distributed, therefore we used nonparametric tests to analyse outcomes before and after treatment. Comparisons before and after were performed using the Wilcoxon signed-rank test for paired data. We conducted a Mann–Whitney U test to compare outcomes between continuers and discontinuers. A statistically significant change was determined by a $p$ value less than 0.05.

**Results**

**Baseline patient characteristics**

In total, 84 patients started HDLAI during the study period. Three patients were lost to follow up and two patients died during the study period. Neither death was considered to be associated with HDLAI treatment. Baseline patient characteristics and reasons for HDLAI initiation are shown in Table 1.

**Haloperidol initiation and discontinuation**

Antipsychotic prescribed immediately before HDLAI, reasons for HDLAI discontinuation and antipsychotic prescribed immediately after HDLAI are shown in Table 2.

At 1 year, 28 patients (33%) remained on treatment (Figure 2). Median survival time for the whole group was 235 days [95% confidence interval (CI) 145–303 days]. Among the group, 77 (92%) patients received at least one monthly maintenance dose of HDLAI. The median monthly maintenance dose for the total cohort was 75 mg: 87.5 mg for continuers and 75 mg for discontinuers.

**Adverse effects**

The following adverse effects were reported in the patients who discontinued treatment because of adverse effects: Extrapyramidal side effects (EPSEs) (62%), restlessness (14%), weight gain (10%), hypersalivation (10%), lack of sleep (5%), sexual dysfunction (5%), constipation (5%), urinary incontinence (5%), cessation of menstruation (5%), discomfort (5%), fatigue (5%), pain (5%), abscess at injection site (5%), skin allergy (5%), chest pain (5%), sedation (5%), reduced sensation in hands (5%).

**Predictors for discontinuation with haloperidol**

Of all variables screened in the univariate analysis ethnicity, nonadherence to previous treatment and illness duration were significantly associated with treatment discontinuation. The
Table 1. Baseline patient characteristics and reasons for HDLAI initiation.

| Characteristic                        | Total cohort \((n = 84)\) | Discontinued \((n = 56)\) | Continued \((n = 28)\) |
|---------------------------------------|---------------------------|---------------------------|------------------------|
|                                       | \(n\) (%)                 | \(n\) (%)                 | \(n\) (%)              |
| Age at initiation (years)             |                           |                           |                        |
| Mean [SD]                             | 40.5 (11.7)               | 39.5 (11.5)               | 42.5 (12.1)            |
| Median (min, max)                     | 41 (20, 70)               | 38.5 (20, 64)             | 43 (22, 70)            |
| Sex                                   |                           |                           |                        |
| Male                                  | 43 (51)                   | 29 (52)                   | 14 (50)                |
| Female                                | 41 (49)                   | 27 (48)                   | 14 (50)                |
| Ethnicity                             |                           |                           |                        |
| White                                 | 20 (24)                   | 9 (16)                    | 11 (39)                |
| Black                                 | 51 (61)                   | 38 (68)                   | 13 (46)                |
| Other                                 | 13 (15)                   | 9 (16)                    | 4 (14)                 |
| Diagnosis                             |                           |                           |                        |
| Schizophrenia                         | 49 (58)                   | 32 (57)                   | 17 (60)                |
| Schizoaffective disorder              | 17 (20)                   | 9 (16)                    | 8 (28)                 |
| Bipolar affective disorder            | 8 (10)                    | 7 (13)                    | 1 (4)                  |
| Other                                 | 10 (12)                   | 8 (14)                    | 2 (8)                  |
| Duration of illness (years)           |                           |                           |                        |
| Mean [SD]                             | 14.2 (10.7)               | 12.9 (10.2)               | 16.7 (11.4)            |
| Median (min, max)                     | 10.5 (0, 40)              | 9 (0, 40)                 | 14 (2, 40)             |
| Considered treatment resistant        |                           |                           |                        |
| Yes                                   | 35 (42)                   | 24 (43)                   | 11 (39)                |
| No                                    | 49 (58)                   | 32 (57)                   | 17 (61)                |
| Previous use of HDLAI                 |                           |                           |                        |
| Yes                                   | 11 (13)                   | 7 (12)                    | 4 (14)                 |
| No                                    | 73 (87)                   | 49 (84)                   | 24 (86)                |
| Initiation regimen                    |                           |                           |                        |
| Loaded                                | 52 (62)                   | 35 (63)                   | 17 (61)                |
| Not loaded                            | 19 (23)                   | 13 (23)                   | 6 (21)                 |
| Loading not required                  | 13 (15)                   | 8 (14)                    | 5 (18)                 |
| Reasons for HDLAI initiation          |                           |                           |                        |
| Patient request                       | 5 (6)                     | 0                         | 5 (18)                 |
| Prior poor adherence                  | 36 (43)                   | 27 (48)                   | 9 (32)                 |
Table 1. (Continued)

| Characteristic                  | Total cohort (n = 84) | Discontinued (n = 56) | Continued (n = 28) |
|--------------------------------|----------------------|-----------------------|-------------------|
|                                | n (%)                | n (%)                 | n (%)             |
| Prior poor response            | 13 (15)              | 13 (23)               | 0                 |
| Prior poor tolerability        | 14 (17)              | 6 (11)                | 8 (29)            |
| Other reasons                  | 10 (12)              | 7 (13)                | 3 (11)            |
| Not stated                     | 6 (7)                | 3 (5)                 | 3 (11)            |

HDLAI, haloperidol decanoate long-acting injection; SD, standard deviation.

Table 2. Antipsychotic prescribed immediately before haloperidol decanoate long-acting injection (HDLAI), reasons for HDLAI discontinuation and antipsychotic prescribed immediately after HDLAI.

| Antipsychotic prescribed immediately before haloperidol (n = 84) | n (%) |
|-----------------------------------------------------------------|-------|
| Oral atypical                                                   | 51 (61)|
| Oral typical                                                    | 9 (11)|
| Depot atypical                                                  | 9 (11)|
| Depot typical                                                   | 3 (3)|
| Clozapine                                                       | 5 (6)|
| Antipsychotic polypharmacy                                     | 5 (6)|
| None                                                            | 2 (2)|

Reasons for discontinuation (n = 56)

| Reason                              | n (%) |
|-------------------------------------|-------|
| Adverse effects                     | 21 (25)|
| Poor response                       | 15 (18)|
| Patient choice                      | 17 (20)|
| Other                               | 3 (4)|

Antipsychotic prescribed immediately after haloperidol (n = 56)

| Antipsychotic prescribed           | n (%) |
|------------------------------------|-------|
| Oral atypical                      | 17 (30)|
| Oral typical                       | 6 (11)|
| Depot atypical                     | 11 (20)|
| Depot typical                      | 0     |
| Clozapine                          | 10 (18)|
| Antipsychotic polypharmacy         | 2 (3)|
| No antipsychotic                   | 10 (18)|

Figure 2. Treatment discontinuation during first year of treatment.
CI, confidence interval.

results of the multivariate Cox regression model showed that risk of discontinuation was significantly increased by initiation due to non-adherence (versus other reasons for initiation) and decreased by longer duration of illness (Table 3).

Analyses of hospital admissions and bed days
In total, 65 patients (excluding forensic patients, patients lost to follow up and patients who died) were included in the analyses of bed days and admissions. In our main analysis, there was a significant reduction in the number of admissions in the year after HDLAI initiation compared with the year before (1.4/patient/year to 0.6/patient/year; \( p = 0.0001 \)). There was a nonstatistically significant reduction in mean bed days from 55.6/patient to 45.0/patient (\( p = 0.07 \) for the same period).

Patients who continued (n = 21) HDLAI for a year had a significant reduction in mean bed
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days (53.1 to 4.0; \( p = 0.0002 \)) and hospital admissions (1.5 to 0.2; \( p = 0.0001 \)) after HDLAI, compared with the year before treatment. Discontinuers (\( n = 44 \)) demonstrated a significant reduction in the number of admissions (1.5 to 0.8; \( p = 0.0001 \)) and a nonstatistically significant increase in mean bed days (56.7/patient to 64.5/patient; \( p = 0.8336 \)) for the same period. See Figures 3 and 4. The mean number of bed days between initiation of HDLAI and discharge from the index admission was 51.

**Sensitivity analyses**

In sensitivity analysis 1 (when the entire index admission was included) there was a significant increase in the mean number of bed days (55.6 to 85.7; \( p = 0.007 \)) and a significant reduction in mean hospital admissions (1.4 to 0.5; \( p = 0.0001 \)) in the year following HDLAI initiation compared with the year before. In sensitivity analysis 2 (disregarding the entire index admission) there was a nonstatistically significant increase in mean bed days (22.8 to 45.0; \( p = 0.086 \)) and no change in mean hospital admissions (0.6 to 0.6; \( p = 0.9915 \)).

### Table 3. Cox regression model results.

| Variable                        | Univariate | Multivariate |
|---------------------------------|------------|--------------|
|                                 | HR 95% CI  | \( p \) value| HR 95% CI  | \( p \) value |
| **Ethnicity**                   |            |              |            |              |
| Black                           | 1.62 0.92, 2.83 | 0.094        | 1.70 0.97, 2.99 | 0.065       |
| Other (reference)               | 0          |              |            |              |
| **Reason for initiation**       |            |              |            |              |
| Non-adherence                   | 1.71 1.01, 2.90 | 0.045        | 1.72 1.01, 2.91 | **0.044**   |
| Other reasons (reference)       | 0          |              |            |              |
| **Duration of illness [years]** | 0.89 0.78, 1.01 | 0.068        | 0.88 0.78, 1.00 | **0.050**   |

*For ease of interpretation, HRs are for each 5-year increase in duration of illness (as opposed to 1-year increase). The result translates to 11% reduced risk of discontinuation for 1–5 years duration of illness compared with duration of illness < 1 year or 20% reduction in risk for 6–10 years duration compared with <1 year duration of illness.

HR, hazard ratio; CI, confidence interval.
In this mirror-image study, only a third of patients who started haloperidol remained on it at 1 year. Haloperidol initiation was associated with a significant reduction in the mean number of hospital admissions. There was no change in the mean number of bed days.

The two main reasons for discontinuation were adverse effects and patient choice. EPSs were the most commonly reported adverse effect leading to discontinuation.

Initiation of haloperidol because of nonadherence was associated with an increased risk of treatment discontinuation and increased duration of illness was associated with a decreased probability of discontinuation. Age, diagnosis, sex, ethnicity, initiation regimen or maintenance dose did not predict continuation with treatment.

**Bed days and hospitalizations**

Outcomes in mirror-image studies are strongly influenced by study design. Researchers must decide at which point during the inpatient admission to ‘place’ the mirror: Previous naturalistic studies have included part, all or none of the index admission. In our main analysis, we positioned the mirror at the point of depot initiation and at discharge from the index admission. This method, as described by Taylor and colleagues, is suggested to be a fair assessment, as it assigns all hospital admissions and bed days before initiation of haloperidol to the previous treatment whilst disregarding the remainder of the admission, thus allowing time for development of response to the new treatment. This method assumes that patients respond to the new treatment and are promptly discharged. In the present study, the mean number of bed days during the index admission after HDLAI initiation was similar to the mean bed days in the entire year preceding HDLAI initiation. This means that our main analysis discounted a large number of bed days which might justifiably have been allocated to HDLAI treatment. Hence the decrease in bed days seen in our primary analysis should be viewed within the context of the number of days spent in hospital after HDLAI initiation and before discharge: bed days appear to increase but this increase is seen during the index admission instead of after discharge. This may explain the difference between the findings in our primary analysis compared with both sensitivity analyses, which showed no reduction in bed days. Results for admissions in our primary analysis were supported by the sensitivity analysis, which also included the index admission.
Treatment discontinuation
Long-acting injections (LAIs) do not differ from oral agents in tolerability.5 Previous studies have reported high discontinuation rates with oral haloperidol compared with second-generation agents.6–8 The efficacy and tolerability of HDLAI is comparable with other first generation LAIs.9 Continuation with an antipsychotic medication is a proxy measure for treatment effectiveness.10 Long-term treatment with any medication indicates both a degree of patient tolerability and clinician confidence in the efficacy of treatment. Conversely, poorly tolerated or ineffective treatments are likely to be stopped. Interestingly, a similar proportion discontinued in our group to that reported by McEvoy and colleagues.1 We found that patients who started HDLAI because of nonadherence were more likely to stop treatment within 1 year whilst patients with a longer duration of illness were more likely to remain on treatment. A number of surveys have shown that patients prescribed LAIs understand the benefits of treatment in relapse prevention.11–14 Patients who attend regular appointments for LAIs are more likely than infrequent attendees to believe that stopping maintenance treatment would result in a relapse. It is possible that patients in our study with a longer duration of illness were those who recognise the risks of treatment discontinuation and were thus more likely to adhere to treatment.

Interestingly, lower rates of discontinuation have been reported with paliperidone palmitate at 1 year in a similar population to those in our study.15,16 However, both these studies included patients who were outpatients stabilized on medication, as well as inpatients. A higher discontinuation rate may have been expected in our study, which included only patients admitted to an inpatient unit following a relapse in their mental state.

Strengths of our study
There are two main strengths of our study: the first is that the data collected accurately reflect the medication received by the patient. Many studies collect data from electronic patient notes or from population databases. We collected data on HDLAI prescription and administration from patient notes and prescription charts for patients each time the depot was due. We can therefore be certain that patients received the medication as recorded. The second is that our study did not influence clinical practice and as such, the data demonstrate naturalistic, real-world outcomes.

Limitations
Mirror-image studies by design have some limitations as described by Kishimoto and colleagues17 which would also apply to our study. For example, we did not randomly select patients to participate in the study, there was no control group and neither did we exclude patients who had previously tried HDLAI or clozapine. However, we believe studies such as this one are an accurate reflection of what happens in practice.

We included in our analysis all inpatients who started HDLAI. More than a third of the patients in our sample had either previously tried clozapine or were considered to be treatment resistant. Nonetheless, discontinuation attributed to lack of efficacy was lower than expected, given the rates of treatment resistance in our sample.

We did not collect data on the use of anticholinergic agents because this information was not available for the entire study duration.

Finally, our study included a relatively small number of patients. A similar study in a larger population is warranted.

Implications for practice
HDLAI was associated with good clinical outcomes in patients who continued treatment at 1 year. However, given the high rate of treatment discontinuation, HDLAI is best considered for those who are likely to continue treatment. Our study suggests that patients with a longer duration of illness and those initiated on HDLAI for reasons other than poor adherence are more likely to continue treatment.

Conclusion
HDLAI was associated with a high treatment discontinuation rate. Hospital admissions fell in the year after HDLAI but there was no change in bed days. Our study suggests that patients with a longer duration of illness and patients initiated on HDLAI for reasons other than poor adherence may benefit from HDLAI initiation.
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Conflict of interest statement
DT has received research grants from Sunovion, Janssen and Lundbeck. He has received consultancy honoraria from Otsuka, Allergan, Sunovion, Janssen and Lundbeck. All other authors declare no conflict of interest.

References
1. McEvoy JP, Byerly M, Hamer RM, et al. Effectiveness of paliperidone palmitate vs haloperidol decanoate for maintenance treatment of schizophrenia: a randomized clinical trial. JAMA 2014; 311: 1978–1987.
2. Taylor DM, Sparshatt A, O’Hagan M, et al. Effect of paliperidone palmitate on hospitalization in a naturalistic cohort - a four-year mirror image study. Eur Psychiatry 2016; 37: 43–48.
3. Taylor D and Olofinjana O. Long-acting paliperidone palmitate - interim results of an observational study of its effect on hospitalization. Int Clin Psychopharmacol 2014; 29: 229–234.
4. Royston P, Ambler G and Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. Int J Epidemiol 1999; 28: 964–974.
5. Misawa F, Kishimoto T, Hagi K, et al. Safety and tolerability of long-acting injectable versus oral antipsychotics: a meta-analysis of randomized controlled studies comparing the same antipsychotics. Schizophr Res 2016; 176: 220–230.
6. Kahn RS, Fleischhacker WW, Boter H, et al. Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial. Lancet 2008; 371: 1085–1097.
7. Lieberman JA, Tollesfson G, Tohen M, et al. Comparative efficacy and safety of atypical and conventional antipsychotic drugs in first-episode psychosis: a randomized, double-blind trial of olanzapine versus haloperidol. Am J Psychiatry 2003; 160: 1396–1404.
8. Green AI, Lieberman JA, Hamer RM, et al. Olanzapine and haloperidol in first episode psychosis: two-year data. Schizophr Res 2006; 86: 234–243.
9. Quraishi S and David A. Depot haloperidol decanoate for schizophrenia. Cochrane Database Syst Rev 2000; (2): CD001361.
10. Swartz MS, Perkins DO, Stroup TS, et al. Assessing clinical and functional outcomes in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial. Schizophr Bull 2003; 29: 33–43.
11. Pereira S and Pinto R. A survey of the attitudes of chronic psychiatric patients living in the community toward their medication. Acta Psychiatr Scand 1997; 95: 464–468.
12. Jaeger M and Rossler W. Attitudes towards long-acting depot antipsychotics: a survey of patients, relatives and psychiatrists. Psychiatry Res 2010; 175: 58–62.
13. Goldbeck R, Tomlinson S and Bouch J. Patients’ knowledge and views of their depot neuroleptic medication. Psychiatr Bull 1999; 23: 467–470.
14. Eastwood N and Pugh R. Long-term medication in depot clinics and patients’ rights: an issue for assertive outreach. Psychiatric Bulletin 1997; 21: 273–275.
15. Attard A, Olofinjana O, Cornelius V, et al. Paliperidone palmitate long-acting injection–prospective year-long follow-up of use in clinical practice. Acta Psychiatr Scand 2014; 130: 46–51.
16. Nikolic N, Page N, Akram A, et al. The impact of paliperidone palmitate long-acting injection on hospital admissions in a mental health setting. Int Clin Psychopharmacol 2017; 32: 95–102.
17. Kishimoto T, Nitta M, Borenstein M, et al. Long-acting injectable versus oral antipsychotics in schizophrenia: a systematic review and meta-analysis of mirror-image studies. J Clin Psychiatry 2013; 74: 957–965.