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2018

Early Australian experience in the maintenance of schizophrenia management with 3-monthly paliperidone palmitate

Nagesh B. Pai

University of Wollongong, nagesh@uow.edu.au

Matthew Warden

St Vincent's Hospital

Publication Details

Pai, N. & Warden, M. (2018). Early Australian experience in the maintenance of schizophrenia management with 3-monthly paliperidone palmitate. *Australasian Psychiatry*, 26 (6), 628-634.

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Abstract

Objectives: Real-world experience from a 6-month product familiarization programme (PFP) for 3-monthly paliperidone palmitate in schizophrenia maintenance treatment.

Methods: Prescribers completed an online questionnaire for each patient at enrolment with further questions at second dose (re-supply) stage and a second survey of their overall experience at the end.

Results: Ninety-four patients were enrolled and received a first dose and 23 received a second dose within the 6-month programme; 51.1% had been hospitalised for symptom relapse in the previous 2 years. Reasons for prescribing were convenience of 3-monthly dosing for patients (94.7%) and patient choice (54.6%). Prescribers followed-up at least once-monthly (69.6% cases) and indicated in 48.9% they would consider shared GP care. All patients were satisfied with symptom control and either maintained functioning or showed improvement. Clinicians felt confident with administration and identifying suitable patients and were all 'satisfied' or 'somewhat satisfied' with efficacy and tolerability. All felt patients' treatment goals were either 'met' (81.3%) or 'partly met' (18.7%) and none reported dissatisfaction with relapse prevention.

Conclusions: Convenient 3-monthly dosing was preferred by clinicians and patients, and symptoms were adequately managed. This has the potential to improve adherence and lead to better outcomes as patients only need four intramuscular doses per year.

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Australasian Psychiatry
2018, Vol 26(6) 628–634
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DOI: 10.1177/1039856218789770
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Nagesh Pai Foundation Professor of Psychiatry, Graduate Medicine, Faculty of Science, Health and Medicine, University of Wollongong, Wollongong, NSW, Australia

Matthew Warden Director AIS, St Vincent's Hospital, Melbourne, VIC, Australia

Abstract

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Conclusions: Convenient 3-monthly dosing was preferred by clinicians and patients, and symptoms were adequately managed. This has the potential to improve adherence and lead to better outcomes as patients only need four intramuscular doses per year.

Keywords: schizophrenia, long-acting antipsychotic agents, survey, maintenance therapy, relapse

We report on real-world experience with 3-monthly paliperidone palmitate (INVEGA TRINZA®) from a 6-month Australian product familiarization programme (PFP). PFPs allow the medical profession to evaluate and become familiar with a product.¹ Three-monthly paliperidone palmitate is an injectable antipsychotic agent for the maintenance treatment of schizophrenia in adult patients previously maintained with 1-monthly paliperidone palmitate (INVEGA SUSTENNA®) for at least 4 months.² Treatment was in line with the approved indication and the Australian Approved Product Information.^{1,2}

Antipsychotic medications are the cornerstone of effective management of schizophrenia but treatment continuity is critical, as discontinuation even for short periods can lead to poorer outcomes.³ Non-adherence remains a major problem, leading to a relapse of psychotic symptoms and deterioration of functioning.^{4,5}

Relapse is associated with poorer long-term outcomes, inability to work, psychiatric re-hospitalisation, committing or being a victim of crime, self-harm, substance abuse and suicide.⁵ However, better antipsychotic adherence leads to improved quality of life, and prevention of relapse is a key aspect of current schizophrenia management guidelines.^{3,5}

Long-acting injectable antipsychotic agents have improved adherence compared to oral formulations, by simplifying dosing and reducing relapse.⁵ Patients do not need to remember to take drugs daily and greater transparency means that healthcare professionals can be

Corresponding author:

Nagesh B Pai, Faculty of Science, Health and Medicine, University of Wollongong, Wollongong, NSW 2522, Australia. Email: nagesh@uow.edu.au

alerted and intervene quickly if patients miss their medication. Plasma levels also decrease more slowly with long-acting injectable formulations, reducing the potential speed of a relapse occurring, which also allows earlier intervention.⁵⁻⁷ Less frequent injections allows more time for patients and physicians to address other important treatment objectives such as psychosocial issues, substance abuse, smoking cessation, health maintenance, and vocational rehabilitation.⁸

Paliperidone palmitate (INVEGA TRINZA®) is currently the only 3-monthly antipsychotic formulation approved for the treatment of schizophrenia.⁹ In Phase 3 clinical trials, 3-monthly paliperidone palmitate was more effective than placebo in delaying time to relapse and reducing relapse rates. It was non-inferior to 1-monthly paliperidone palmitate in the proportion of patients that remained relapse-free. Its side-effect profile was similar to 1-monthly paliperidone palmitate and was well tolerated with no new safety concerns.^{10,11} Prior to its approval, long-acting antipsychotics were only available in 2-weekly or 4-weekly formulations.⁹

Methods

The PFP ran for 6 months and included 94 patients, enrolled by 16 prescribing clinicians in six states across Australia. All patients needed to be adequately maintained on 1-monthly paliperidone palmitate for at least 4 months prior to starting 3-monthly paliperidone palmitate. At enrolment, clinicians completed a preliminary online questionnaire for each patient supply request (Table 1). When requesting re-supply (a second dose) they were prompted to answer additional follow-up questions regarding their perception of the patient's experience. A total of 23 patients (25%) received a second dose before the programme ended. At the end of the PFP, each prescriber completed a second survey on their overall experience (Table 2).

No formal protocol was required under Medicines Australia guidance for the conduct of a PFP, as individual patient data was not collected, only aggregated data on the prescriber's experience with the product.¹

Results

Patient characteristics

Of the 94 patients enrolled, 75.5% identified as male and 24.5% female. Participants were aged from 20 to 73 years old (median 43.5 years) and age at diagnosis varied from 14 to 63 years old.

The majority of patients (77.7%) had been maintained on the higher doses of 1-monthly paliperidone palmitate, 100 mg (39.4%), and 150 mg (38.3%). The length of maintenance on 1-monthly paliperidone palmitate varied from the minimum of 4 months to 98 months (mean 28.6±20.1 months); 51.1% of patients had been hospitalised due to symptom relapse in the previous 2 years prior to enrolment.

Patient experience (clinician-reported)

The most prevalent reason for prescribing 3-monthly paliperidone palmitate (94.7%) was 'convenience of 3-monthly dosing for the patient'. In 56.4% of cases the patient chose or requested 3-monthly paliperidone palmitate. In 43.6% the prescriber cited their own preference, and in 21.3% of cases prior poor medication adherence was a factor.

For the majority of patients (68.1%), clinicians reported planned follow-up care at least once-monthly and this figure remained similar (69.6%) when asked again at the re-supply stage. In 48.9% of cases, clinicians said they would consider shared care with a GP.

For all patients at the re-supply stage, clinicians reported that functioning was maintained or in 13.1% of cases functioning was improved. All patients were satisfied ('somewhat satisfied', 'very satisfied' or 'completely satisfied') with the control of their symptoms (Table 3).

Prescriber experience

All clinicians felt confident with the administration of 3-monthly paliperidone palmitate and in identifying suitable patients for treatment. They were all either 'satisfied' (81%) or 'somewhat satisfied' (19%) with efficacy and tolerability. No one reported dissatisfaction with relapse prevention and all felt that the treatment goal for their patients was either 'met' (81.3%) or 'partly met' (18.7%) whilst on 3-monthly paliperidone palmitate. All participants reported being either 'satisfied' (62.5%) or 'somewhat satisfied' (37.5%) with the PFP itself (Table 4).

Discussion and conclusions

The results of these real-world experience surveys indicate a high level of satisfaction and confidence with 3-monthly paliperidone palmitate, as reported by prescribers. Collectively, prescribers felt their patients' treatment goal was met in most cases, patient functioning was maintained or improved in every case, and patients appeared satisfied with symptom control. There were no major relapses or readmissions to hospital, which would allow more opportunity to devote the time needed for psychosocial and other aspects of patient recovery.

It is anticipated that 3-monthly paliperidone palmitate will play a significant role in maintenance treatment for schizophrenia patients by delaying time to relapse and reducing non-adherence, with the potential to improve clinical outcomes and reduce the burden on the healthcare system.^{7,12} It requires less frequent dosing than other currently available antipsychotic agents, as patients only need four injections per year compared to 12 monthly injections or 24 fortnightly injections.² This is could benefit not only stable, high-functioning patients who are likely to find the 3-monthly dosing schedule more user-friendly but an important group who, for logistical, financial, or psychosocial reasons, struggle to access appropriate healthcare and maintain treatment.

Table 1. PFP preliminary survey questions. Prescribers answered questions for each patient at enrolment with further questions when they ordered their second dose

PFP survey questions at enrolment

Patient initials

Patient year of birth

Patient's gender

State/Territory where the patient resides

Patient's age at diagnosis

In the past 2 years, how many hospitalisations due to relapse of schizophrenia symptoms has the patient had?

How long has the patient been maintained on INVEGA SUSTENNA®?

Patient's anticipated start date on INVEGA TRINZA®

What medication did the patient use immediately prior to treatment with INVEGA SUSTENNA® (paliperidone palmitate injectable)?

<Please choose one>

- Aripiprazole
- Asenapine
- Clozapine
- Flupenthixol decanoate
- Fluphenazine decanoate
- Haloperidol decanoate
- Lurasidone
- Olanzapine
- Paliperidone palmitate (oral)
- Quetiapine
- Risperidone
- Ziprasidone
- Zuclopenthixol decanoate
- Other (Please specify)

What was the patient's last INVEGA SUSTENNA® dose? (Prior to initiation on INVEGA TRINZA®)

<Please select one >

- 50 mg
- 75 mg
- 100 mg
- 150 mg

Where was INVEGA SUSTENNA® administered?

<Please select one >

- Deltoid
- Gluteal

Where will the first dose of INVEGA TRINZA® be administered? <Please select one >

- Deltoid
- Gluteal

Why have you prescribed INVEGA TRINZA® to this patient?

<You can select more than one>

- The convenience of the 3 monthly administration to you
- The convenience of the 3 monthly dosing for the patient
- Patient choice/request
- Prior poor medication adherence
- Other (please specify)

(Continued)

Table 1. (Continued)***PFP survey questions at enrolment***

After initiation on INVEGA TRINZA[®], what is your preference for frequency of follow-up (from you as prescribing physician) before the next dose?

<Please select one >

- Won't be providing ongoing care
- Every 2 weeks
- Every month
- Every 2 months
- At next dose (3 months)

After initiation of INVEGA TRINZA[®], how soon would you consider shared care with a GP?

<Please select one >

- I would not consider shared care with a GP
- After dose 1
- After dose 2
- After dose 3

QUESTIONS AT RE-ORDER STAGE (SECOND DOSE)

In which setting will the second dose of INVEGA TRINZA[®] be administered?

<Please select one >

- Community mental health centre
- Primary care
- Private clinic
- Hospital
- Other

3 months after initiation of INVEGA TRINZA[®], what is your preference for frequency of follow-up (from you as prescribing physician) for ongoing management?

<Please select one >

- Won't be providing on-going care
- Every 2 weeks
- Every month
- Every 2 months
- At next dose (3 months)

How satisfied are your patients with the ongoing control of their symptoms with INVEGA TRINZA[®]?

<Please select one >

- Not at all satisfied
- Slightly satisfied
- Somewhat satisfied
- Very satisfied
- Completely satisfied

Please select as appropriate. Following administration of the first dose the patient has:

- Not maintained his/her functioning
- Maintained his/her functioning
- Slightly improved his/her functioning
- Significantly improved his/her functioning

Table 2. End of PFP survey questions. Each prescriber answered these questions at the end of the programme regarding their own experience

SURVEY QUESTIONS

How confident were you in identifying whether a patient was suitable for INVEGA TRINZA® use?

<Please select one>

- Completely confident
- Very Confident
- Confident
- Slightly confident
- Not at all confident

How confident are you with the administration of INVEGA TRINZA®? <Please select one >

- Completely confident
- Very Confident
- Confident
- Slightly confident
- Not at all confident

How satisfied are you with the effectiveness (efficacy and tolerability) of INVEGA TRINZA®?

<Please select one>

- Very satisfied
- Somewhat satisfied
- Neither satisfied nor dissatisfied
- Somewhat dissatisfied
- Very dissatisfied

How satisfied are you with relapse prevention (reduced risk of rehospitalisation) with INVEGA TRINZA®? <Please select one>

- Very satisfied
- Somewhat satisfied
- Neither satisfied nor dissatisfied
- Somewhat dissatisfied
- Very dissatisfied

Collectively, was your treatment goal for the patients met during this programme? <Please select one>

- Met
- Partially met
- Not met

How comfortable are you with patient management, given the longer dosing interval of INVEGA TRINZA®? <Please select one>

- Very comfortable
- Somewhat comfortable
- Neither comfortable nor uncomfortable
- Somewhat uncomfortable
- Very uncomfortable

Overall satisfaction: On a scale of 1 to 10, how likely are you to recommend INVEGA TRINZA® to a colleague for use in their patients? <Please provide a rating between 1 and 10 (1 not at all likely to 10 extremely likely)

Please rate your level of satisfaction with the INVEGA TRINZA® Product Familiarisation Program?

<Please select one >

- Very satisfied
- Somewhat satisfied
- Neither satisfied nor dissatisfied
- Somewhat dissatisfied
- Very dissatisfied

Table 3. PFP primary survey: patient response at second dose stage (n=23)

	Completely satisfied	Very satisfied	Somewhat satisfied	Slightly satisfied	Not satisfied
Do patients appear satisfied with ongoing symptom control after first dose?	4.5%	81.9%	13.6%	0	0
	Significantly improved functioning	Slightly improved functioning	Maintained functioning	Not maintained functioning	NA
Patient functioning after first dose	0	13.6%	86.4%	0	NA

Table 4. End of PFP survey responses: prescriber satisfaction, comfort and confidence (n=16)

	Very satisfied	Somewhat satisfied	Neither satisfied nor dissatisfied	Somewhat dissatisfied	Very dissatisfied
Satisfaction with relapse prevention	56.25%	37.5%	6.25%	0	0
Satisfaction with effectiveness	81.25%	18.75%	0	0	0
Satisfaction with PFP	62.5%	37.5%	0	0	0
	Completely confident	Very confident	Confident	Slightly confident	Not at all confident
Confidence in identifying suitable patients	18.75%	69.75%	12.5%	0	0
Confidence with product administration	18.75%	62.5%	12.5%	6.25%	0
	Very comfortable	Somewhat comfortable	Neither comfortable nor uncomfortable	Somewhat uncomfortable	Very uncomfortable
Comfort with patient management	62.5%	37.5%	0	0	0
	Met	Partially met	Not met	NA	NA
Was treatment goal met?	81.25%	18.75%	0	NA	NA
	1-6	7	8	9	10
Overall satisfaction: Likely to recommend to a colleague (Rating: 1 - not at all likely, 10 - extremely likely)	0	6.25%	37.5%	31.25%	25.0%

When choosing an antipsychotic, shared decision-making that considers patient preference and choice is important.³ In other surveys from the Phase 3 clinical trials of 3-monthly paliperidone palmitate, both patients and physicians preferred long-acting injectables over oral formulations, and physicians showed a greater preference for 3-monthly versus 1-monthly dosing.¹³ The findings of this Australian PFP

confirmed that these were also significant factors when prescribing this medication within this setting.

A significant number of specialists indicated a willingness to share patient management with GPs. For patients who are stable and well controlled, this would reduce costs and increase convenience as the number of specialist visits

could be reduced. However, 3-monthly dosing should not be the only reason for less frequent follow-up. Patients should still continue to see a mental healthcare professional as often as required, based on the management needs of the individual patient.³ Given that treatment will be lifelong, it is highly likely that patients will eventually transition to their GP for ongoing care.

It is important to select the right patients for this treatment and prescribers reported that they felt confident with this. Those already adequately maintained on the 1-monthly formulation may be less likely to have previously unknown side-effect issues. There was no new or increased severity of side effects, compared to 1-monthly preparations.¹⁰ Maintaining a regular follow-up schedule would also ensure that any adverse effects are identified and managed early.³ Acute side effects are expected to be less of a problem where patients have already been adequately maintained on other paliperidone formulations.¹⁴

As the enrolment period for PFPs may not exceed 6 months, the majority (75%) of patients only received one dose of 3-monthly paliperidone palmitate during the time frame allowed.¹ PFP guidelines also place limits on the data that can be collected and only aggregated patient data could be used in this study.¹ However, these data have been collected from the use of this medicine outside the constraints of randomised controlled trial conditions. Such real-world evidence is increasingly being recognised as a valuable asset in clinical decision making.¹⁵ These findings, taken together with the available evidence base, suggest that 3-monthly paliperidone palmitate has the potential to improve adherence and clinical outcomes for schizophrenia patients.

Acknowledgements

The PFP and its associated prescriber surveys are a Janssen Neuroscience initiative supported by Janssen Australia and New Zealand (Janssen-Cilag Pty Ltd). The authors wish to thank all clinicians who participated in the PFP and completed the PFP surveys. The authors thank Rachel Johnatty (PhD, CMPP) of Biocommunic (Australia) for providing editorial and writing assistance, which was funded by Janssen Australia and New Zealand in accordance with Good Publication Practice (GPP3) guidelines (<http://www.ismpp.org/gpp3>).

Disclosure

NP received speakers' honoraria from Lundbeck, Otsuka, MSD, Pfizer, Janssen-Cilag, Eli Lilly, AstraZeneca, and Servier. NP served on Advisory Boards for Lundbeck, Otsuka, and Janssen-Cilag. MW received honoraria from Janssen-Cilag.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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