

**5.10 PALIPERIDONE PALMITATE,
I.M. injection (modified release) 700 mg (as
palmitate) in pre-filled syringe,
I.M. injection (modified release) 1000 mg (as
palmitate) in pre-filled syringe,
Invega Hafyera[®],
Janssen-Cilag Pty Ltd.**

1 Purpose of submission

- 1.1 The Category 2 submission requested an Authority Required (Streamlined) listing for paliperidone palmitate 6 monthly long-acting injection (PP6M) for the maintenance treatment of schizophrenia in adult patients who have been adequately treated with the 1-month paliperidone palmitate injectable product (PP1M) for at least four months or the 3-month paliperidone palmitate injectable product (PP3M) for at least one 3-month injection cycle.
- 1.2 Listing was requested on the basis of a cost-minimisation analysis versus PP3M, with PP1M as a secondary comparator.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Adult patients with schizophrenia who have been adequately treated with PP1M for at least four months or PP3M following at least one 3-month injection cycle.
Intervention	PP6M (INVEGA HAFYERA [®]) is a gluteal intramuscular injection in dose strengths of 700 mg or 1000 mg paliperidone administered once every 6 months.
Comparator	Primary comparator: PP3M Secondary comparator: PP1M
Outcomes	Primary endpoints: Proportion of patients who have not relapsed at the end of the 12-month DB Phase; Time to relapse during 12-month DB Phase Secondary endpoints: Change from baseline of DB Phase during 12 months in: PANSS total score PANSS subscale/factor scores CGI-S PSP Safety evaluations
Clinical claim	PP6M as a maintenance treatment is non-inferior in efficacy and safety compared to PP3M in adult patients with schizophrenia who have been adequately treated and stabilised with PP1M for at least four months, or PP3M following at least one 3-month injection cycle.

Source: Table 1.1, p16 of the submission. Abbreviations: DB = double blind; PANSS = Positive and Negative Symptom Scale for Schizophrenia; CGI-S = Clinical Global Impression-Severity; PP6M = Paliperidone palmitate 6-monthly; PP3M = Paliperidone palmitate 3-monthly; PP1M = Paliperidone palmitate 1-monthly; PSP = Personal and Social Performance

2 Background

Registration status

- 2.1 PP6M was registered on the Australian Register of Therapeutic Goods (ARTG) on 10 February 2022.
- 2.2 The ARTG registered indication in the product information (PI) was ‘for the maintenance treatment of schizophrenia in adult patients who have been adequately treated with the 1-month paliperidone palmitate (PP) injectable product for at least four months or the 3-month PP injectable product following at least one 3-month injection cycle.’

Previous PBAC consideration

- 2.3 This is the first submission to the PBAC for PP6M. The PBAC recommended PP1M for the maintenance treatment of schizophrenia in adults at its November 2010 meeting, which was PBS-listed on 1 December 2011. At its November 2016 meeting, the PBAC recommended PP3M for the maintenance treatment of schizophrenia in patients who have been adequately treated with PP1M for at least four months, which was PBS-listed on 1 April 2017. The PBAC has previously accepted non-inferiority between PP3M and PP1M (paragraphs 7.2 and 7.3, page 10; PP3M Public Summary Document (PSD) November 2016).

3 Requested listing

- 3.1 The submission requested the following restriction for PP6M.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
PALIPERIDONE PALMITATE 700 mg/3.5 mL modified release injection, 3.5 mL syringe 1 g/5 mL modified release injection, 5 mL syringe	1	0	\$2147.34	INVEGA Janssen-Cilag HAFYERA® Australia Pty Ltd
Category/Program:	General Schedule			
PBS indication:	Schizophrenia			
Treatment phase:	Initial and continuing			
Restriction:	Authority Required – Streamlined			
Clinical criteria:	Patient must have previously received and be stabilised on PBS-subsidised paliperidone three-monthly injection for at least one injection cycle or Patient must have previously received and be stabilised on PBS-subsidised paliperidone once-monthly injection for at least 4 consecutive months			
Prescriber criteria:	Medical Practitioners For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.			

Source: Table 1.8, pp35-36 of the submission.

- 3.2 The requested restriction was consistent with the ARTG registered indication.

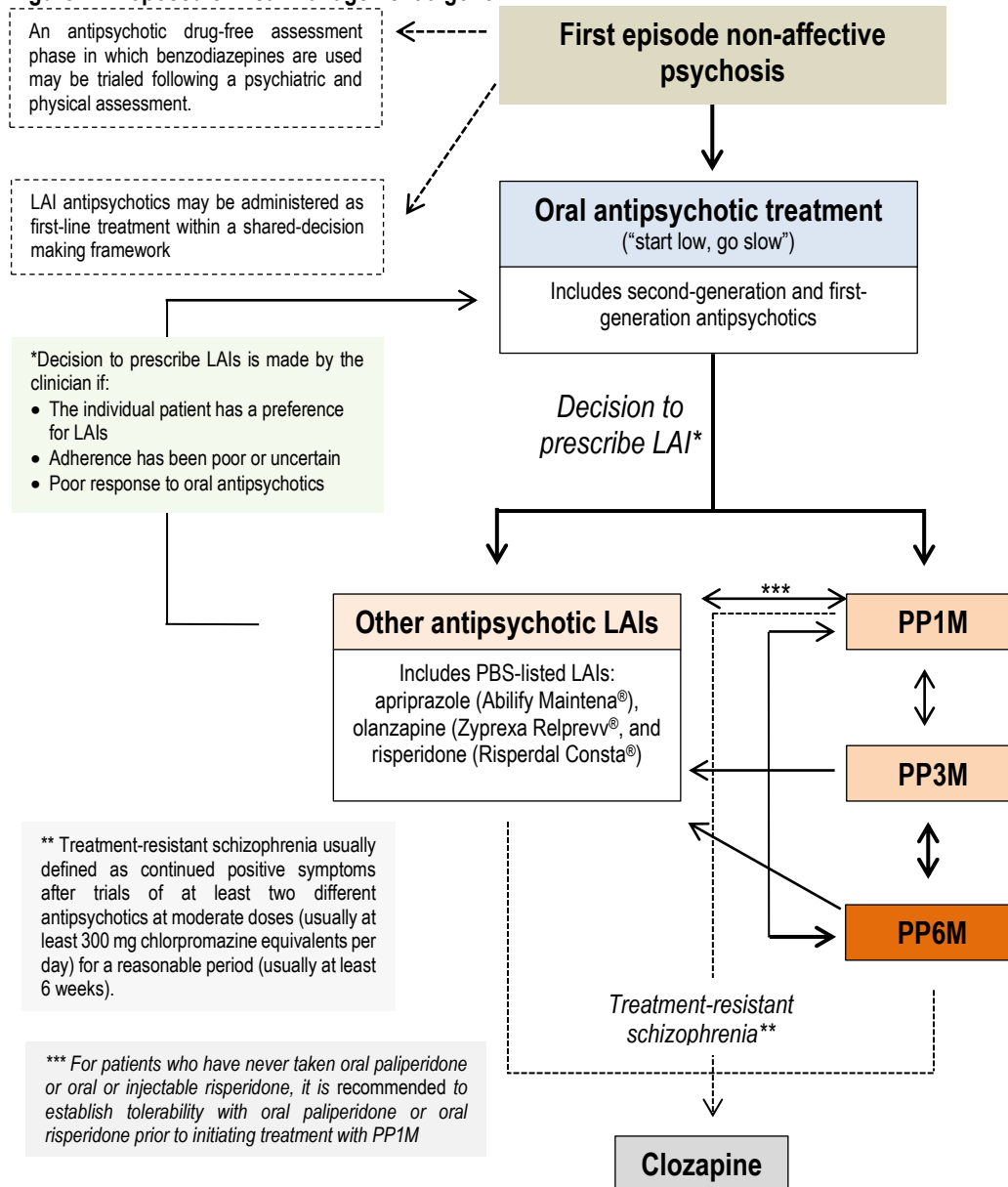
- 3.3 The submission proposed clinical criteria to transition patients from PP3M or PP1M to PP6M. The PBAC considered these criteria would be reasonable since treatment with PP6M was demonstrated in the clinical evidence to be non-inferior in effectiveness and safety to PP3M and PP1M.
- 3.4 The requested restriction was considered simple in terms of the time required for finalisation, given that it is based on the current restriction for paliperidone.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

- 4.1 Schizophrenia is a severe, chronic, relapsing psychiatric illness characterised by disturbances in speech, perception, cognition, volition and emotion.
- 4.2 The submission proposed that the clinical management algorithm for patients with schizophrenia following the PBS listing of PP6M will remain largely unchanged apart from the availability of PP6M as an additional maintenance treatment option for schizophrenia patients who have been adequately treated with PP3M for at least one 3-month injection cycle or PP1M for at least 4 months. For patients adequately treated with PP3M, a decision would be made by the treating clinician in consultation with the patient and/or their carer whether to switch to PP6M or remain on PP3M. The proposed treatment algorithm is shown below.
- 4.3 Paliperidone palmitate (PP) is an atypical neuroleptic antipsychotic; paliperidone is 9-hydroxyrisperidone. The 6-month formulation dissolves slowly after intramuscular injection and the plasma concentrations are predicted to reach maximum on Day 33 and 35 for the 700 mg and 1000 mg doses respectively. This results in therapeutic concentrations being sustained over a period of 6 months.

Figure 1: Proposed clinical management algorithm



Source: Figure 1.2p 31 of the submission.

5 Comparator

- 5.1 The submission nominated PP3M as the main comparator. The main argument provided in support of this nomination was that clinicians advised that the patients who were stabilised on PP3M were most likely to use PP6M.
- 5.2 The submission nominated PP1M as a supplementary comparator on the basis that switching from PP1M to PP6M would be consistent with the PI, but was less likely to happen in practice.

- 5.3 The PBAC considered that these comparators were appropriate. The PBAC considered that while it is unlikely that patents would switch from other antipsychotic long-acting injections (LAIs) to PP6M, these should also be considered as near market comparators.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

- 6.1 There was no hearing for this item.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (2) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described how long-acting antipsychotics have resulted in benefits for patients including greater treatment stability, fewer visits to the doctor, and shifting the treatment focus from compliance to the improving of quality of life and pursuing goals such as stable employment. However, some comments described some risks of long acting treatment including fewer visits to the doctor which may affect rapport, reduce opportunities for patients to seek support when it is required, and reduce the monitoring of patients' symptoms. The comments emphasised that the treatment focus with PP6M should be on understanding how to manage symptoms proactively, psychoeducation, and building clinician-patient trust and rapport.
- 6.3 The PBAC noted the advice received from the Mental Illness Fellowship of Australia clarifying the likely use of PP6M in clinical practice. The PBAC specifically noted the advice that the use of PP6M may reduce stigma, improve compliance, provide greater convenience, and empower the patient with choice and control.

Clinical trials

- 6.4 The submission was based on one head-to-head trial comparing PP6M to PP3M (PSY3015).
- 6.5 The details of the trial presented in the submission are provided in the table below.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
PSY3015	Janssen. A Double-blind, Randomized, Active-controlled, Parallel-group Study of Paliperidone Palmitate 6 Month Formulation	EudraCT Number: 2017-001941-28

Source: Table 2.4, p42 of the submission.

- 6.6 The key features of the randomised trial are summarised in the table below.

Table 3: Key features of PSY3015

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
PSY3015	702	R, DB, MC, 12 months	Low	Adults with schizophrenia	Proportion of patients without relapse at 12 months. Time to relapse during the trial. PANSS total score. PANSS subscale scores. CGI-S. PSP.

Source: Tables 2.8 and 2.17, pp 54 and 70 of the submission. Abbreviations: DB = double blind; MC = multi-centre; R = randomised. PANSS=Positive and Negative Symptom Scale for Schizophrenia, CGI-S=Clinical Global Impression-Severity, PSP=Personal and Social Performance

- 6.7 The trial was designed as a non-inferiority trial with a non-inferiority margin of -10% in the proportion of patients free of relapse at 12 months. This non-inferiority margin was the same as that used in the trial comparing PP1M with PP3M (PSY3011), which was previously considered by PBAC.
- 6.8 The trial characteristics and eligibility criteria were consistent with the proposed listing. The characteristics of the patients and the treatment setting were similar to the Australian setting.
- 6.9 The treatment details in PSY3015 are shown below.

Table 4: Treatment exposure in PSY3015

Safety population	PSY3015	
	PP6M (N=478)	PP3M (N=224)
Duration of exposure, days		
Mean (SD)	329.8 (86.97)	336.4 (80.89)
Median	365.0	365.0
Range	(11; 480)	(27; 557)
Mean Dose (mg eq) (DB)		
N	478	224
Mean (SD)	855.6 (150.05)	442.2 (87.57)
Median	1000.00	525.00
Range	(700; 1000)	(350; 525)

Source: Table 2.14, p67 of the submission. DB = double-blind phase of the trial.

- 6.10 The dosing and duration of the proposed medicine and comparator matched the respective PIs. A high but similar proportion of patients across both trial arms received psychotropic medications, with > 85% of patients in either treatment arm having received at least one prior psychotropic medication.

Comparative effectiveness

- 6.11 The results of the trial are shown in the table below.

Table 5: Results for key outcomes in PSY3015

	PP3M N = 224	PP6M N = 478	Difference (95% CI)
Relapses, n (%)	11 (4.9%)	36 (7.5%)	NR
% Relapse Free	94.8%	91.9%	-2.9% (-6.8, 1.1)
Relapse defined by#			
Self-harm, Suicide or Violence	0	1 (0.2%)	
Hospitalisation	6 (2.7%)	11 (2.3%)	
Suicidal or Homicidal Ideation	1 (0.4%)	2 (0.4%)	
Increase in PANSS Total Score	5 (2.2%)	21 (4.4%)	
PANSS Total Score - Change from Baseline to 52 weeks			
Mean (SD)	-1.6 (7.4)	-1.8 (8.9)	-0.1 (-1.44, 1.19)
Median (range)	-2.0 (-20-45)	-3.0 (-22-79)	
Clinical Global Impression of Severity (CGI-S) - Change from Baseline to 52 weeks			
Mean (SD)	0.0 (0.63)	0.0 (0.7)	0.0 (-0.11, 0.09)
Median (range)	0.0 (-2-3)	0.0 (-2-5)	
Personal & Social Performance Scale (PSP) - Change from Baseline to 52 weeks			
Mean (SD)	1.1 (8.11)	1.0 (7.1)	-0.2 (-1.27, 0.97)
Median (range)	0.0 (-30-25)	-0.2 (-41-23)	

Source: Table 19, CSR p93; Table 20, CSR p95; Table 26, CSR pp105-6; NR = not reported

Reasons are non-exclusive.

- 6.12 The proportion of patients who were relapse-free after 12 months was 91.9% in the PP6M group and 94.8% in the PP3M group. The submission stated that as the lower bound of the 95% CI (-6.8%) was greater than the pre-specified non-inferiority margin of -10%, PP6M is non-inferior to PP3M for the proportion of patients who remain relapse-free at 12 months. The PBAC noted that the pre-specific non-inferiority margin was met, and considered that PP6M was non-inferior to PP3M in terms of the proportion of patients who were relapse-free after 12 months.
- 6.13 The mean (SD) change in PANSS total scores was -1.8 (8.92) in the PP6M group and -1.6 (7.40) in the PP3M group and the difference of the LS means (95% CI) between the treatment groups (PP6M-PP3M) in PANSS total scores was -0.1 (-1.44, 1.19), supporting the claim of non-inferiority. The results were consistent across the doses tested and across the subgroups examined in the trial.
- 6.14 The results from the PSY3015 study were highly similar to those of the PSY3011 study, which compared PP1M to PP3M and was considered by the PBAC at its November 2016 meeting (paragraph 6.6, PP3M, PSD, November 2016 PBAC meeting). The PBAC noted that there did not appear to be material differences in the effectiveness of PP1M, PP3M and PP6M: the proportion of patients taking PP6M who were relapse-free in the PSY3015 study (91.9%) was similar to that of the PSY3011 study (PP1M 90.0%, PP3M 91.5%); the difference in favour of PP3M in the PSY3015 study was due to a slightly better result with PP3M in the PSY3015 study (94.8% vs 91.5%).

Comparative harms

- 6.15 The adverse events as reported in the trial are shown below.

Table 6: Summary of key adverse events in PSY3015

	OL Phase N = 838	PP3M DB Phase N = 224	PP6M DB Phase N = 478
All TEAE, n (%)	341 (40.7%)	131 (58.5%)	297 (62.1%)
Serious TEAE, n (%)	23 (2.7%)	15 (6.7%)	24 (5.0%)
TEAE Leading to Treatment Withdrawal, n (%)	31 (3.7%)	6 (2.7%)	16 (3.3%)
TEAE Leading to Death, n (%)	1 (0.1%)	2 (0.9%)	1 (0.2%)
Injection Site Pain	72 (8.6%)	9 (4.0%)	37 (7.7%)
All Injection Site AEs#	89 (10.6%)	11 (4.9%)	59 (12.3%)
Parkinsonian Tremor	11 (1.3%)	2 (0.9%)	9 (1.9%)
Dyskinesia	11 (1.3%)	2 (0.9%)	6 (1.3%)
Parkinsonism	NR	2 (0.9%)	6 (1.3%)
Patients with increased QTC during DB Phase, n/N (%)	NA	4/215 (1.9%)	11/463 (2.4%)

Source: Table 33, CSR p122; Table 34, CSR p122; Table 35, CSR p124; CSR p135; Table 42, CSR p139, Table 52, CSR p159. Abbreviations: DB = double-blind; OL = Open-Label; QTC = corrected QT interval; TEAE = treatment emergent adverse event, NR = not reported.

Including injection site pain, swelling, induration, erythema, haemorrhage, nodule, oedema, and leg pain.

- 6.16 The events in the double-blind (DB) phase may underestimate the frequency of events in clinical use because of the withdrawal of patients who found the injections unpleasant in the Open-Label (OL) phase. The higher frequency of injection site reactions with the use of PP6M was likely due to the greater volume that was injected, but the rate was still relatively low. More patients in the PP6M group showed increased QT intervals (2.4% vs 1.9%), however the finding was infrequent and may not reflect any real difference.
- 6.17 The submission provided additional data on potential safety concerns beyond those identified in the clinical trials from its latest Periodic Safety Update Report (PSUR) for all strengths of PP. No significant new safety concerns were identified in the PSUR, however data for PP6M was limited.

Benefits/harms

- 6.18 As the claim was for non-inferiority, information on the benefits and harms was not presented in the evaluation.

Clinical claim

- 6.19 The submission described PP6M as non-inferior in terms of effectiveness and safety compared with PP3M.
- 6.20 The evaluation noted that as the PBAC has already accepted the non-inferiority of PP3M and PP1M, it would be reasonable to extend the equivalence to included PP6M. The PBAC agreed with the evaluation.
- 6.21 The submission claimed reduced carer burden, improved equity of access for patients in remote areas, and improved adherence. The PBAC noted the submission and Pre-Sub-Committee Response provided a brief description of qualitative studies to support these statements.
- 6.22 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonably supported.

Economic analysis

6.23 The submission presented a cost-minimisation analysis. The key assumptions and components of the cost-minimisation approach are summarised in the table below.

Table 7: Key components and assumptions of the cost-minimisation analysis

Component	Claim or assumption
Therapeutic claim: effectiveness	Effectiveness is assumed to be non-inferior
Therapeutic claim: safety	Safety is assumed to be non-inferior
Evidence base	Direct comparison of proposed medicine and main comparator
Equi-effective doses	1 injection of PP6M 700mg = 2 injections of PP3M 350mg 1 injection of PP6M 1000mg = 2 injections of PP3M 525mg
Direct medicine costs	Equivalent over 48 weeks
Other costs or cost offsets	none

Source: Table 3.1, p120 of the submission

6.24 The equi-effective doses were estimated as 1 injection of PP6M 700 mg = 2 injections of PP3M 350 mg and 1 injection of PP6M 1000 mg = 2 injections of PP3M 525 mg over 48 weeks. The equi-effective doses used in the cost-minimisation analysis were taken from results of the double-blind phase of the PSY3015 trial and are consistent with the draft PI.

6.25 No additional cost or cost offsets were included in the analysis. This approach was consistent with the cost-minimisation analysis of PP3M vs PP1M (paragraph 6.20, PP3M, PSD, November 2016 PBAC meeting).

6.26 The submission proposed a flat pricing structure for PP6M 700 mg and PP6M 1000 mg, consistent with the pricing structure for PP3M 350 mg and 525 mg, (AEMP of \$993.06 for both strengths) which equates to an AEMP of \$1,986.12 (i.e. \$993.06 x 2).

6.27 The results of the cost-minimisation analysis are shown in the table below.

Table 8: Results of the cost-minimisation analysis

	PP6M (700/1000 mg)	PP3M (350/525 mg)
Route of administration	Intramuscular injection	Intramuscular injection
Frequency of administration	Every 6 months (i.e., 24 weeks)	Every 3 months (i.e., 12 weeks)
Number of prescriptions per 48-week period	2	4
AEMP per prescription	\$1,986.12	\$993.06
Total cost of drug therapy over 48 weeks	\$3,972.24	\$3,972.24
Other costs (e.g., MBS)	\$0.00	\$0.00
Net difference in treatment cost over 48 weeks	\$0.00	

Source: Table 3.2, p122 of the submission. Abbreviations; PP6M = paliperidone palmitate 6-monthly; PP3M = paliperidone palmitate 3-monthly.

Estimated PBS usage & financial implications

6.28 This submission was not considered by DUSC. The submission used a market share approach, assuming that PP6M would only substitute for PP3M and PP1M, and not for other long-acting injectable (LAI) antipsychotics. Although the availability of a 6 monthly injection might encourage switching from other LAIs, the PBAC considered

that the number of patients was likely to be small. The PBAC considered that a market share approach was appropriate.

6.29 The submission assumed no overall market expansion, which may be reasonable. The assumptions concerning substitution rates of PP1M by PPP6M were tested in sensitivity analyses.

6.30 To estimate the substitution of PP3M by PP6M, the annual substitution rate of PP1M by PP3M since PP3M was first PBS listed was used. The submission proposed that it is expected that PP6M will substitute PP1M to a smaller extent than PP3M. In the financial estimates model, it assumed that the substitution rate of PP1M by PP6M would be 20% of the substitution rate of PP3M by PP6M. Based on the experience of substitution of PP1M by PP3M as shown in the data, the PBAC considered this approach was reasonable. The PBAC considered, as stated in the submission, that it would be unlikely for a large proportion of patients to switch directly from PP1M to PP6M. The PBAC considered it would also be very unlikely to have patients switch from other LAIs to PP6M, as discussed above.

6.31 The key inputs for the financial estimates are shown in the table below.

Table 9: Key inputs for financial estimates

Parameter	Value applied and source			Comment
Number of prescriptions for each relevant strength of PP1M and PP3M	Services Australia PBS/RPBS dispensed services data.			Reasonable
Extrapolation of PP1M and PP3M prescriptions	Linear trend analysis and log trend analysis for PP1M and PP3M prescriptions respectively.			Reasonable – trends selected on best curve fit
Uptake rate	year	PPM1	PPM3	Sponsor assumption based on substitution rate of PBS items and PP1M by PP3M - reasonable based on analysis although not possible to verify
	1	1.1%	5.5%	
	2	3.2%	15.9%	
	3	4.1%	20.6%	
	4	4.9%	24.5%	
	5	5.1%	25.6%	
6	5.4%	26.8%		
Cost of therapy and patient co-payments	PBS items numbers and DHS.			Reasonable

Source: Tables 4.1, 4.3 p124 and 126 of the submission.

6.32 The estimated use and financial implications are shown in the table below.

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Table 10: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of PP6M scripts dispensed ^a (total 700 mg and 1000mg)	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹
Estimated financial implications of PP6M						
Cost to PBS/RPBS less copayments (\$)	2 ²	2 ²	2 ²	2 ²	2 ²	2 ²
Estimated financial implications for PP1M and PP3M						
Cost to PBS/RPBS less copayments (\$)	2 ²	2 ²	2 ²	2 ²	2 ²	2 ²
Net financial implications						
Net cost to PBS/RPBS (\$)	2 ²	2 ²	2 ²	2 ²	2 ²	2 ²

Source: Tables 4.4, 4.6, 4.12 and 4.15, pp127-133 of the submission.

^a Assuming 2 scripts per year as estimated by the submission.

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² \$0 to < \$10 million

6.33 The total cost to the PBS/RPBS of listing PP6M was estimated to be \$0 to < \$10 million in Year 6, and a total of \$30 million to < \$40 million in the first 6 years of listing. If the assumed substitution rate is correct, the submission estimated that there would be a net cost saving in the first 6 years of listing due to fewer mark-ups and fees for the 6 monthly injection.

6.34 The main source of uncertainty for the financial estimates presented was the assumed substitution rate of PP3M and PP1M by PP6M. The results of the sensitivity analysis are shown below.

Table 11: Results of sensitivity analysis

Net impact for the health budget	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 1-6
	2022	2023	2024	2025	2026	2027	2022-27
Base case	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹
20% increase in substitution rate	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹
	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
20% reduction in substitution rate	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹	-\$1 ¹
	-20.0%	-20.0%	-20.0%	-20.0%	-20.0%	-20.0%	-20.0%

Source: Table 4.19, p 135 of the submission.

The redacted values correspond to the following ranges:

¹ \$0 to < \$10 million

Quality Use of Medicines

6.35 The submission stated that, as was done for PP1M and PP3M, each of the patients, medical practitioners, nurse practitioners and pharmacists will be provided with appropriate education, resources, and support from the sponsor to promote the appropriate prescribing and use of PP6M.

7 PBAC Outcome

- 7.1 The PBAC recommended the Authority Required (Streamlined) listing of PP6M for the maintenance treatment of schizophrenia in adult patients who have been adequately treated with PP1M for at least four months or PP3M for at least one 3-month injection cycle. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of PP6M would be acceptable if it were cost-minimised to PP3M and PP1M for the same indication.
- 7.2 The PBAC considered the equi-effective doses to be 1 injection of PP6M 700 mg = 2 injections of PP3M 350 mg and 1 injection of PP6M 1000 mg = 2 injections of PP3M 525 mg over 48 weeks. The PBAC noted that the equi-effective doses used in the cost-minimisation analysis were taken from results of the double-blind phase of the PSY3015 trial and were consistent with the doses in the approved PI.
- 7.3 The PBAC noted consumer comments were supportive of the listing of PP6M given the various benefits resulting from patients having fewer injections. However, the PBAC noted the concerns raised that a reduction to two appointments per year might jeopardise the development of clinician-patient rapport and reduce the focus on supporting the psychosocial needs of the patient. The PBAC considered that clinicians are well-placed to assess the appropriateness of this treatment interval for their patients.
- 7.4 The PBAC considered PP3M to be the appropriate main comparator with PP1M as a secondary comparator. The PBAC considered that while it is unlikely that patients would switch from other PBS listed antipsychotic LAIs to PP6M, these should also be considered as near market comparators.
- 7.5 The PBAC considered that the results from the PSY3015 study were highly similar to those of the PSY3011 study, which compared PP1M to PP3M and was considered by the PBAC at its November 2016 meeting (paragraph 6.6, PP3M PSD, November 2016 PBAC meeting). The PBAC noted that there did not appear to be material differences in the effectiveness of PP1M, PP3M and PP6M such that the proportion of patients taking PP6M who were relapse-free in the PSY3015 study (91.9%) was similar to that of the PSY3011 study (PP1M 90.0%, PP3M 91.5%).
- 7.6 The PBAC accepted the proposed flat pricing structure for PP6M 700 mg and PP6M 1000 mg, noting that this was consistent with the pricing structure for PP3M 350 mg and 525 mg.
- 7.7 The PBAC agreed with the submission assumption that there would be no overall expansion of the market and considered that listing PP6M should result in a nil cost to government, since it is likely that patients would switch from PP3M or PP1M at equivalent cost. The PBAC noted that the availability of a 6-monthly injection might encourage switching from other LAI antipsychotics to PP6M, but considered that the number of patients switching from other LAI antipsychotic drugs was likely to be small, and its financial impact was considered to be minimal.

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- 7.8 The PBAC considered that the restriction for PP6M should be consistent with the restriction of PP3M with the inclusion of the criterion of being stabilised on PP3M for at least one 3-month injection cycle. The PBAC advised that there should be flow-on changes to allow patients to transition from PP6M to PP3M or PP1M if they have been stabilised on PP6M for at least one 6-month injection cycle.
- 7.9 The PBAC recommended that the Early Supply Rule should not apply to PP6M, noting that the Early Supply Rule does not apply to PP1M and PP3M.
- 7.10 The PBAC advised that the PP6M is suitable for prescribing by nurse practitioners within a shared care model, consistent with the listings for PP3M and PP1M.
- 7.11 The PBAC recommended that PP6M should not be treated as interchangeable on an individual patient basis with any other drugs as it is the first long acting injectable antipsychotic with a 6-month duration of action.
- 7.12 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because PP6M is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over PP3M or PP1M, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 7.13 The PBAC noted that this submission was not eligible for an Independent Review as it was recommended.

Outcome:

Recommended

8 Recommended listing

8.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
PALIPERIDONE					
paliperidone 700 mg/3.5 mL modified release injection, 3.5 mL syringe	NEW	1	1	0	Invega Hafyera
paliperidone 1 g/5 mL modified release injection, 5 mL syringe	NEW	1	1	0	Invega Hafyera
Restriction Summary [new based on 6832] / Treatment of Concept: [new based on 6832]					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED) [new/existing code]					
Indication: Schizophrenia					

Public Summary Document – March 2022 PBAC meeting

	Clinical criteria:
	Patient must have previously received and be stabilised on PBS-subsidised paliperidone three-monthly injection for at least one cycle OR
	Patient must have previously received and be stabilised on PBS-subsidised paliperidone once-monthly injection for at least 4 consecutive months
	Administrative Advice: Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.
	Administrative Advice: Patient dosage is to be determined as per the dose transition table in the Product Information based on the maintenance dose of paliperidone once monthly injection.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.