INVEGA SUSTENNA® (paliperidone palmitate 1-month)
Dosing - Conversion to INVEGA SUSTENNA from Oral Antipsychotics

General Information[a]

There are no systematically collected data that address switching patients from other antipsychotics to PP1M or concerning concomitant administration of other antipsychotics.

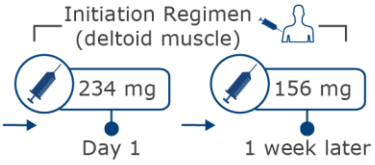
Dosing[a-g]

Tolerability Testing[a]

Patients who have never taken oral paliperidone or oral/injectable risperidone → Tolerability should be established with oral paliperidone or oral risperidone before initiating PP1M

PP1M Initiation Regimen[b,c]

Previous oral antipsychotics can be gradually discontinued at the time of initiation of treatment with PP1M



Switching From Oral Paliperidone[c-e]

- Patients previously stabilized on different doses of paliperidone ER tablets can attain similar paliperidone steady-state exposure during maintenance treatment with monthly doses of PP1M.[c-e]

Oral Paliperidone ER (Once Daily)[e]	Recommended PP1M Initiation Regimen (234 mg on day 1 and 156 mg on day 8 via deltoid injection)	PP1M Injection (Every 4 Weeks in the Deltoid or Gluteal Muscle)[e]
3 mg		39-78 mg
6 mg		117 mg
9 mg		156 mg
12 mg		234 mg

Switching From Oral Risperidone[d,f]

- Population PK simulations were conducted to determine which dose levels of oral risperidone result in similar PK to the PP1M 78-234 mg dose levels at steady state.[d,f]

Oral Risperidone (Once Daily)[f]	Recommended PP1M Initiation Regimen (234 mg on day 1 and 156 mg on day 8 via deltoid injection)	PP1M Injection (Every 4 Weeks in the Deltoid or Gluteal Muscle)[f]
1 mg		39 mg
2 mg		78 mg
3 mg		117 mg
4 mg		156 mg
6 mg		234 mg

Switching From Oral or Injectable Antipsychotics[g]

- Using data from an open-label study and postmarketing databases, relapse rates were compared following a switch from RLAI to PP1M versus switch from oral or LAI antipsychotics to PP1M.
  - Incidences of symptom worsening, or relapse were similar when patients switched from RLAI to PP1M versus oral or other LAI antipsychotics to PP1M.
  - In the postmarketing review, no specific period of vulnerability following a switch to PP1M could be identified; the authors recommended monitoring for symptoms of relapse for several weeks following a switch to a new antipsychotic regimen.

Click on the following links to related sections within the document: Switching from Oral Paliperidone, Switching from Oral Risperidone, and Switching From Atypical Antipsychotics.

Please refer to the product labeling for additional information pertaining to dose equivalency or conversion.

Abbreviations: ER, extended release; LAI, long-acting injectable; PK, pharmacokinetics; PP1M, paliperidone palmitate 1-month; RLAI, risperidone long-acting injectable.

[a]Samtani (2011).[1] [b]Dose equivalency has not been established between INVEGA SUSTENNA and other antipsychotics other than those summarized below. [c]Gopal (2010).[2] [d]Russu (2017).[3] [e]Data on File (2020).[4] [f]Russu (2018).[5] [g]Gopal (2014).[6]

DOSAGE STRENGTH INFORMATION

Doses of paliperidone palmitate extended-release injectable suspension may be expressed in milligram equivalents of paliperidone (active moiety) or milligrams of paliperidone palmitate. Dosage information in this response has been converted to mg of paliperidone palmitate to reflect the commercially available dosage strengths in the United States. The conversion factor from mg eq. to mg is 1.56.

- INVEGA SUSTENNA doses expressed as 39, 78, 117, 156, and 234 mg of paliperidone palmitate are equal to 25, 50, 75, 100, and 150 mg eq. of paliperidone, respectively.

SWITCHING FROM ORAL PALIPERIDONE

Patients previously stabilized on different doses of paliperidone extended-release tablets can attain similar paliperidone steady-state exposure during maintenance treatment with monthly doses of INVEGA SUSTENNA see Table: Doses of Paliperidone Extended-Release and INVEGA SUSTENNA Needed to Attain Similar Exposure to Active Moiety at Steady-State.

Doses of Paliperidone Extended-Release and INVEGA SUSTENNA Needed to Attain Similar Exposure to Active Moiety at Steady-State[4]

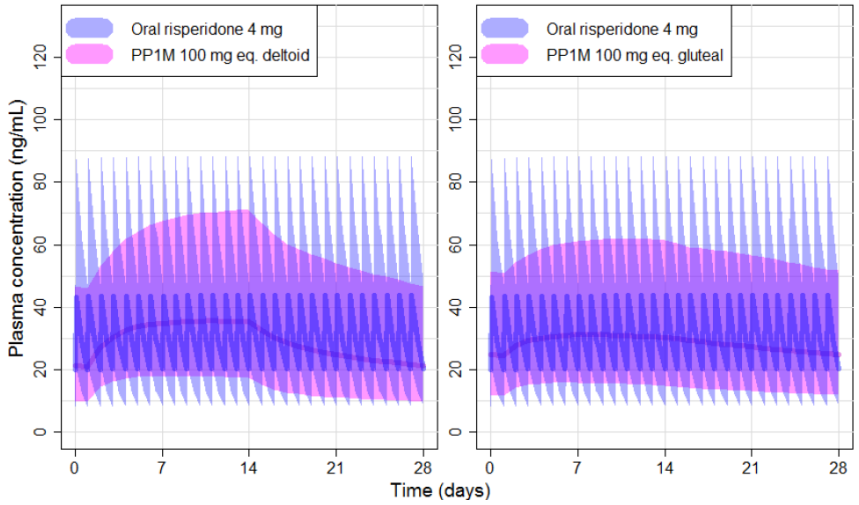
Formulation	Oral Pali ER	INVEGA SUSTENNA Injection
Dosing Frequency	Daily	Every 4 Weeks (deltoid or gluteal)
Dose	3 mg	39 – 78 mg
	6 mg	117 mg
	9 mg	156 mg
	12 mg	234 mg
Abbreviations: ER, extended release.		

The recommended initiation regimen for INVEGA SUSTENNA (234 mg on day 1 and 156 mg on day 8 via deltoid injection) is required for this transition. However, no oral antipsychotic supplementation is required.

SWITCHING FROM ORAL RISPERIDONE

Population PK simulations[3,5] were conducted to determine which dose levels of oral risperidone (RIS) result in similar pharmacokinetics to the INVEGA SUSTENNA 78-234 mg dose levels at steady-state. For oral RIS, active moiety concentrations (risperidone and 9-OH-risperidone [paliperidone]) were compared to paliperidone concentrations for INVEGA SUSTENNA (Figure: Steady State Plasma Concentrations - Oral Risperidone 4 mg Compared to Paliperidone Palmitate 156 mg via Deltoid and Gluteal Injections).

Steady State Plasma Concentrations - Oral Risperidone 4 mg Compared to Paliperidone Palmitate 156 mg via Deltoid and Gluteal Injections[3]



Abbreviations: PP1M, paliperidone palmitate 1 month.
Time axis shown as day 0 to 28 to enable comparison between pharmacokinetic steady-states of the two compounds.
Steady State: Oral risperidone (from day 14 to day 42 following daily dosing); PP1M (from week 61 to 65 following every 4 week injections starting with initiation doses of 234 mg and 156 mg on days 1 and 8, respectively).
PP1M dose of 100 mg eq. is equal to 156 mg of paliperidone palmitate.

The results from the pharmacokinetic simulations suggest that patients stabilized with oral RIS can attain similar steady-state exposure to active moiety during maintenance treatment with monthly doses of INVEGA SUSTENNA administered via deltoid or gluteal injection. These results are summarized in the Table: Doses of RIS and INVEGA SUSTENNA Needed to Attain Similar Exposure to Active Moiety at Steady-State. The recommended initiation regimen for INVEGA SUSTENNA (234 mg on day 1 and 156 mg on day 8 via deltoid injection) is required for this transition. However, no oral antipsychotic supplementation is required.

Doses of RIS and INVEGA SUSTENNA Needed to Attain Similar Exposure to Active Moiety at Steady-State[5]

Formulation	Oral RIS[a]	INVEGA SUSTENNA Injection
Dosing Frequency	Daily	Every 4 Weeks (deltoid or gluteal)
Dose	1 mg	39 mg
	2 mg	78 mg
	3 mg	117 mg
	4 mg	156 mg
	6 mg	234 mg

Abbreviations: RIS, risperidone.
[a]Conversion factor: 1 mg oral RIS = 39 mg INVEGA SUSTENNA. Note: The conversion does not take into account the potential effects of CYP2D6 inhibitors (i.e., paroxetine, sertraline or fluoxetine) or inducers (i.e., carbamazepine) on active moiety concentrations.

SWITCHING FROM ATYPICAL ANTIPSYCHOTICS

PALMFlex

PALMFlex is an international, prospective, 6-month, open-label study conducted to assess the efficacy and safety of treatment with flexibly dosed INVEGA SUSTENNA in adult patients

with acute or nonacute schizophrenia who failed previous treatment with other antipsychotics.[7-9]

Study Design/Methods

- After tapering off oral antipsychotics over ≤4 weeks, INVEGA SUSTENNA was initiated at 234 mg on day 1 and 156 mg on day 8 (±2 days), both administered IM in the deltoid muscle.
  - Tolerability testing with paliperidone ER 3 mg/day for at least 2 days was conducted in patients without previous exposure to risperidone or paliperidone.
  - Patients receiving clozapine within 3 months of trial initiation were not eligible to participate.
- For patients receiving long-acting injectables, the first INVEGA SUSTENNA dose (78-234 mg) was administered in place of the next scheduled depot injection.
- Flexible INVEGA SUSTENNA doses of 78-234 mg were administered monthly thereafter (±7 days).

Results

PALMFlex - Efficacy and Safety Outcomes

Lead Author/Patient Population	Efficacy	Safety
Hargarter (2015)[7] reported results in patients with acute schizophrenia switched from oral antipsychotics (ITT, n=212).	• Patients transitioned from oral antipsychotics primarily due to lack of efficacy (45.8%) and lack of compliance (34.9%). • Patients received a mean modal INVEGA SUSTENNA maintenance dose of 168 mg for a mean treatment period of 136.9 days. • Overall, 66.7% of patients experienced a ≥30% improvement in PANSS total scores from baseline to LOCF endpoint while 43.5% of patients achieved a ≥50% improvement. • From baseline to LOCF endpoint, significant improvements were observed in mean PANSS total (-31.0; *P*<0.0001) and mean CGI-S (-1.5; *P*<0.0001) scale scores. Significant reductions in PANSS total were observed as early as day 8.	• At least one TEAE was experienced in 63.7% of patients with the majority rated mild-to-moderate in nature by investigators (89.1%). • The most common TEAEs (≥5%) were injection site pain (13.7%), insomnia (10.8%), psychotic disorder (10.4%), headache (6.1%) and anxiety (6.1%). • Potentially prolactin-related TEAEs occurred in 5.7% of the total patient population. • Mean ESRS total scores, while low at baseline, significantly declined during the trial (3.8 baseline to 2.3 LOCF endpoint; *P*<0.0001). • Mean changes in baseline to LOCF endpoint weight and BMI change were 2.6 kg and 0.9 kg/m^2, respectively. Forty patients (22.5%) experienced a ≥7% increase in body weight.
Schreiner (2014)[8] reported results in patients with symptomatic non-acute schizophrenia switched from oral antipsychotics (risperidone, paliperidone ER, olanzapine, aripiprazole, quetiapine, haloperidol, amisulpride, quetiapine	• Mean modal INVEGA SUSTENNA maintenance dose: 158.2 mg • Main reasons for switch to INVEGA SUSTENNA included: patient's wish (43.7%), lack of efficacy (24.3%), lack of compliance (23.3%) and lack of tolerability (8.8%).	• The most common TEAEs (≥5%) were injection site pain (12.3%), insomnia (8.6%), anxiety (6.7%), psychotic disorder (6.1%) and headache (5.6%). • Most TEAEs were mild or moderate in intensity and did not require a change in dosage. • While protocol-based laboratory tests were not conducted during the

fumarate, sertindole and ziprasidone) (ITT efficacy/safety, n=593).	• At LOCF endpoint, the following percentages of patients had a ≥20% improvement in PANSS total scores: *Total population* (n=589): 64.0% Patients switched for lack of efficacy (n=143): 61.5% Patients switched for other reasons (n=446): 64.8% • From baseline to LOCF endpoint, significant improvements in mean PANSS total change scores were observed: *All patients* (n=589): -11.7 (*P*<0.0001) Patients switched for lack of efficacy (n=143): -12.1 (*P*<0.0001) Patients switch for other reasons(n=446): -11.6 (*P*<0.0001)	study, 18 patients (3.0%) reported at least one potentially prolactin-related TEAE, 4 patients (0.7%) reported hyperprolactinemia and 7 patients (1.2%) reported a potentially prolactin-related TEAE as well as hyperprolactinemia. • A significant reduction in ESRS scores, from baseline to LOCF endpoint, was observed (2.8 to 1.6; *P*<0.0001). • Mean weight and BMI increased 1.2 kg and 0.4 kg/m^2, respectively, from baseline to LOCF endpoint. Eighty-one patients (15.4%) experienced a ≥7% increase in weight (baseline to LOCF endpoint).
Abbreviations: BMI, body mass index; CI, confidence interval; CGI-S, clinical global impression-severity; ESRS, extrapyramidal symptom rating scale; ITT, intent-to-treat; LAI, long-acting injectable; LOCF, last-observation-carried-forward; PANSS, Positive and Negative Syndrome Scale; TEAE, treatment-emergent-adverse-event.		

Gopal et al (2014)[6] analyzed outcomes from the PALMFlex trial to compare relapse rates following a switch from risperidone long-acting injectable (RLAI) to INVEGA SUSTENNA versus a switch from oral or other LAI antipsychotics to INVEGA SUSTENNA. Incidences of symptom worsening or relapse appeared similar between the switch from RLAI (17.9%) or other LAI antipsychotics (11.4% to 16.7%) to INVEGA SUSTENNA as well as the switch from oral risperidone (12.3%) or other oral antipsychotics (19.3%) to INVEGA SUSTENNA.

PALMFlex Subanalyses

An additional subanalysis reporting outcomes in non-acute patients switched from oral atypical antipsychotic monotherapy has been referenced for your convenience.[10]

Sub-Group Analysis in Chinese Patients

A sub-group analysis of a 13-week, open-label, single arm, interventional study reported efficacy and safety of INVEGA SUSTENNA following a switch from oral antipsychotics in Chinese patients with acute schizophrenia. This analysis has been referenced for your convenience.[11]

SWITCHING FROM CLOZAPINE

Maia-de-Oliveira et al (2015)[12] reported two cases of clozapine-resistant schizophrenia successfully treated with INVEGA SUSTENNA. Details are provided in the Table: Descriptive Patient Characteristics.

Descriptive Patient Characteristics[12]

Case	Age of Schizophrenia Onset (years)	Number of Prior Antipsychotics	Prior Clozapine Dose	Number of Admissions to Psychiatric Ward	INVEGA SUSTENNA Dose	Time of Follow-Up with Good Outcome (Months)
19-yr-old female	17	4	400 mg	2	117 mg	10
26-yr-old male	20	5	600 mg	4	Initial: 117 mg; Final: 156 mg	9

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 26 March 2025.

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