XEPLION® paliperidone palmitate

TREVICTA® paliperidone palmitate prolonged release suspension for injection

Johnson&Johnson

SAVE THE BRAIN

DOSING AND ADMINISTRATION GUIDE

RECOMMENDATIONS FOR SWITCHING TO XEPLION®

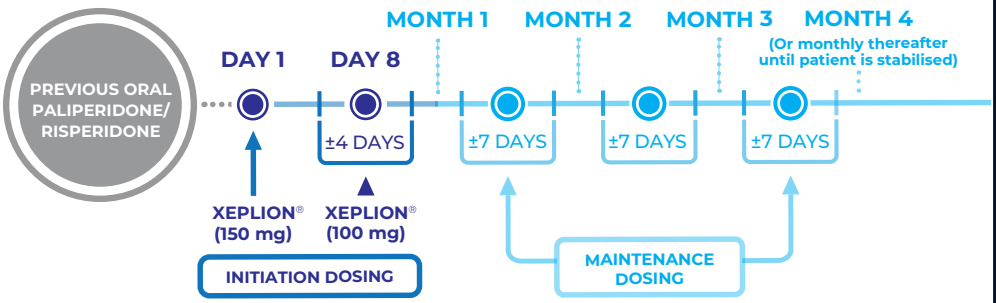
The 1-week initiation regimen is recommended for patients taking an oral antipsychotic but it is not required in patients at steady state on a long-acting injectable antipsychotic[1]

From oral therapy to XEPLION®	From injectables to XEPLION®
• The 1-week initiation dosing is required[1] • Previous oral antipsychotics can be gradually discontinued at the time of initiation of treatment with XEPLION®[1]	• When switching patients currently at steady-state on a long-acting injectable antipsychotic, initiate XEPLION® in place of the next scheduled injection[1] • The 1-week initiation dosing is not required[1]

It is recommended to establish tolerability* with oral paliperidone or oral risperidone prior to initiating treatment with XEPLION®[1]

*** In patients who have never taken oral paliperidone, or oral or injectable risperidone**

XEPLION®
paliperidone palmitate



When switching patients from risperidone LAT, initiate XEPLION® in place of the next scheduled risperidone LAT administration. The 1-week initiation dosing regimen including the intramuscular injections (Day 1 and 8, respectively) is not required.[1]

The recommended monthly maintenance dose is 75 mg; some patients may benefit from lower or higher doses within the recommended range of 50 to 150 mg based on individual patient tolerability and/or efficacy.[1]

XEPLION® is indicated for the treatment of schizophrenia and for the prevention of recurrence of symptoms of schizophrenia, For patients who have never taken oral paliperidone, or oral or injectable risperidone, it is recommended to establish tolerability with oral paliperidone or oral risperidone prior to initiating treatment with XEPLION® [1]

SWITCHING FROM ORAL RISPERIDONE OR ORAL PALIPERIDONE TO XEPLION®

The 1-week initiation regimen is recommended for patients taking oral risperidone or oral paliperidone[1]

Previous oral antipsychotics can be gradually discontinued at the time of initiation of treatment with XEPLION®[1]

Patients previously stabilised on different doses of oral risperidone or paliperidone ER can attain similar XEPLION® steady-state exposure during maintenance treatment with the following doses:[3,4]

Oral risperidone	Paliperidone ER	XEPLION®
2 mg/day	4 mg/day	50 mg eq/month
3 mg/day	6 mg/day	75 mg eq/month
4 mg/day	9 mg/day	100 mg eq/month
6 mg/day	12 mg/day	150 mg eq/month

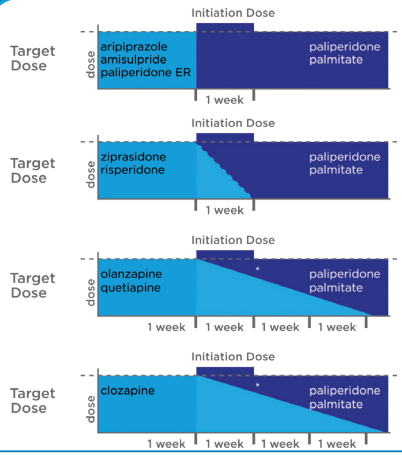
Adjustments of the maintenance dose may be made monthly[1]

SWITCHING FROM OTHER **ORAL ANTIPSYCHOTICS** TO **XEPLION®**

The 1-week initiation dosing regimen is required in patients taking an oral antipsychotic[1]

Oral antipsychotics can be gradually discontinued at the time of initiation of treatment with XEPLION®

There are no systemic data to specifically address switching patients from other antipsychotics to XEPLION®, but Stahl SM, 2013 has recommended the following tapering strategies[4]



	No tapering required.
	Risperidone and ziprasidone can be tapered off over a period of 1 week due to the risk of withdrawal symptoms such as insomnia.
	Clinical experience has shown that olanzapine and quetiapine should be tapered off over a period of 3 - 4 weeks due to the risk of withdrawal symptoms associated with cholinergic, histaminergic and alpha-1 receptor blocking.
	Clozapine should always be tapered gradually, over a period of 4 weeks or more.

* Benzodiazepine or anticholinergic medication administered during reduction of olanzapine and clozapine, can alleviate side effects

SWITCHING FROM **RISPERIDONE LONG-ACTING INJECTION (LAI) TO XEPLION®**

Initiate XEPLION® therapy in place of the next schedule injection and then monthly thereafter, with no need for the 1-week initiation dose[1,4]

	Risperidone LAI	XEPLION®
Dosing frequency	Every 2 weeks	Monthly
Dose	25	50
	37,5	75
	50	100
	-	150

XEPLION® OFFERS SIMPLE, ONCE-MONTHLY DOSING[1]

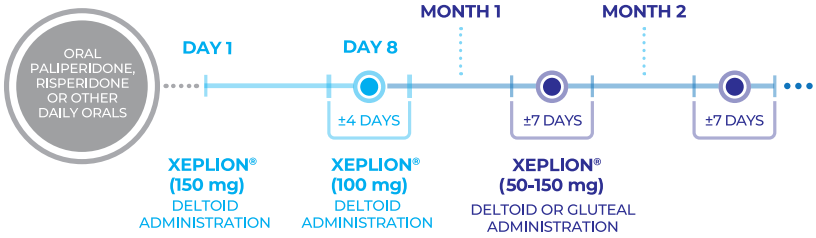
Needle selection is weight dependent

Patient < 90kg		Patient ≥ 90kg
 Deltoid	 Gluteal	 Deltoid or gluteal
 Blue hub	 Grey hub	 Grey hub
23G × 1" (25.4 mm x 0.64 mm)	22G × 1½" (38.1 mm x 0.72 mm)	22G × 1½" (38.1 mm x 0.72 mm)

When switching from oral antipsychotics, the first two doses of XEPLION® should be administered into the deltoid muscle only

1

Initiate XEPLION® as follows:



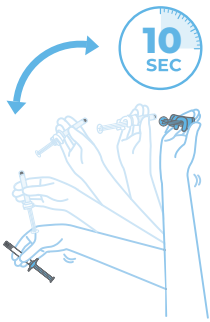
- **1st initiation dose:** 150 mg on treatment Day 1 into a deltoid muscle
- **2nd initiation dose:** 100 mg on treatment Day 8 (1 week later) into a deltoid muscle
- **3rd dose:** should be administered 1 month after the 2nd initiation dose into either a deltoid or gluteal muscle*

The recommended monthly maintenance dose is 75 mg; some patients may benefit from higher or lower doses within the recommended range of 50 mg to 150 mg based on individual patient tolerability and/or efficacy.

* When making dose adjustments, the prolonged release characteristics of XEPLION® should be considered, as the full dose adjustment may not be evident for several months[1]

2

Preparing for administration[5]



It is important to shake the syringe correctly to ensure a homogeneous suspension:

1. Position the syringe with the tip pointing upwards

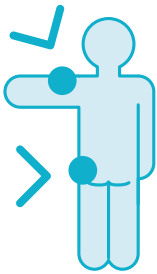
2. Vigorously shake with a loose wrist for at least 10 seconds

If more than 5 minutes pass before administration, shake vigorously again for at least 15 seconds to re-suspend.

The contents of the pre-filled syringe should be visually inspected for foreign matter and discolouration prior to administration.

3

Administering XEPLION®[1]



Inject slowly and deep into the muscle. Administration should be in a single injection. Do not administer the dose in divided injections.

Do not administer intravascularly or subcutaneously.

* The recommended initiation of XEPLION® is with a dose of 150 mg on treatment Day 1 and 100 mg one week later, both administered in the deltoid muscle.

4

Disposal[1]

Any unused product or waste material should be disposed of in accordance with local requirements.

XEPLION® is for single use only. Any unused portion should be discarded.

The shelf life of XEPLION® is 2 years.

Do not use after the expiry date on the label.

WHAT IF MY **PATIENT MISSES** A **DOSE** OF **XEPLION®?**

XEPLION® should be administered intramuscularly once every month.[1,4]

- It is recommended that the 2nd initiation dose of **XEPLION®** be given 1 week after the 1st dose. To avoid a missed dose, patients may be given the 2nd dose 2 days before or after the 1-week (Day 8) time point.[1,4]

- The 3rd and subsequent administrations after the initiation regimen are recommended to be given monthly.[1,4]

- To avoid a monthly missed dose, patients may be given the dose up to 7 days before or after the monthly time point.[1,4]

If the target date for the second **XEPLION®** dose (Day 8 ± 2 days) is missed, the recommended reinitiation depends on the length of time which has elapsed since the patient's 1st dose.[1,4]

If a subsequent dose is missed, clear recommendations are provided for proceeding with treatment.

For patients who miss their 2nd initiation dose[1]

If 2nd initiation dose is missed and the time since the 1st initiation dose is:	Action
< 4 weeks from 1st injection	• XEPLION® 100 mg should be administered as soon as possible into a deltoid muscle • A 3rd injection of XEPLION® 75 mg should be administered in either a deltoid or gluteal muscle 5 weeks after the 1st injection
4 - 7 weeks from 1st injection	If 4 to 7 weeks have elapsed since the first injection of XEPLION®, resume dosing with two injections of 100 mg in: 1. a deltoid injection as soon as possible. 2. another deltoid injection one week later, 3. resumption of the normal monthly cycle of injections in either the deltoid or gluteal muscle of 50 mg to 150 mg based on individual patient tolerability and/or efficacy
> 7 weeks from 1st injection	• XEPLION® dosing should be initiated following the recommended initiation schedule, including administrations on Days 1 and 8.

For patients who miss a monthly maintenance dose[1]

If a monthly maintenance dose is missed and the time since the last dose is:	Action
1 month - 6 weeks	• The previously stabilised dose of XEPLION® should be administered as soon as possible followed by monthly intervals
> 6 weeks - 6 months	**For patients stabilised with doses of 50 mg to 100 mg:** 1. a deltoid injection as soon as possible at the same dose the patient was previously stabilised on 2. another deltoid injection (same dose) one week later (day 8) 3. resumption of the normal monthly cycle of injections in either the deltoid or gluteal muscle of 50 mg to 150 mg based on individual patient tolerability and/or efficacy **For patients stabilised with a dose of 150 mg:** 1. a deltoid injection as soon as possible at the 100 mg dose 2. another deltoid injection (same dose) one week later (day 8) 3. resumption of the normal monthly cycle of injections in either the deltoid or gluteal muscle of 50 mg to 150 mg based on individual patient tolerability and/or efficacy
> 6 months	• Initiate dosing as described for the initial recommended initiation of XEPLION®

HOW DO I INITIATE **XEPLION®** IN **SPECIAL POPULATIONS?**

Patients with renal impairment [1]

XEPLION® has not been systematically studied in patients with renal impairment.

For patients with mild renal impairment (creatinine clearance ≥ 50 mL/min to < 80 mL/min), the recommended initiation dose of XEPLION® is 100 mg on treatment Day 1, and 75 mg 1 week later, both administered into a deltoid muscle. The recommended monthly maintenance dose is 50 mg with a range of 50 mg to 100 mg based on individual patient tolerability and/or efficacy.

XEPLION® is not recommended in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min).

Patients with hepatic impairment [1]

Based on experience with oral paliperidone, no dose adjustment is required in patients with mild or moderate hepatic impairment.

Paliperidone has not been studied in patients with severe hepatic impairment

Elderly patients with schizophrenia [1]

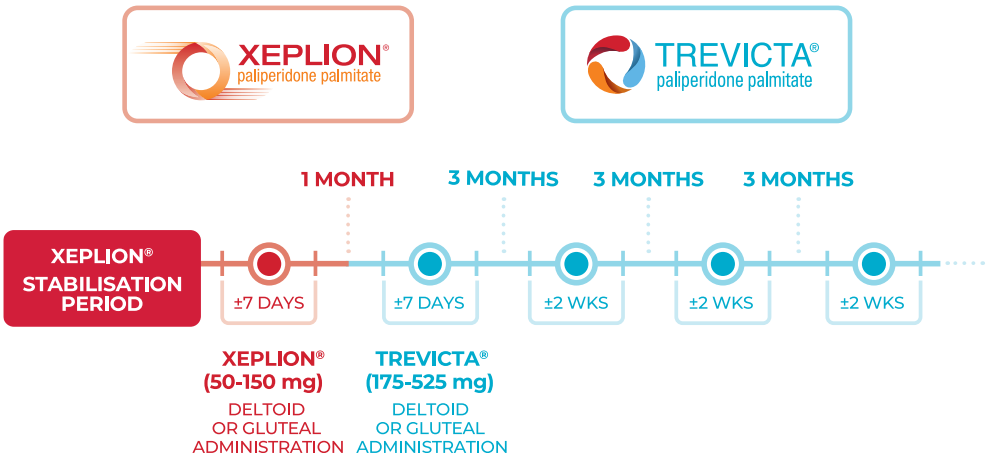
In general, recommended dosing of XEPLION® for elderly patients with normal renal function is the same as for younger adult patients with normal renal function.

For elderly patients with reduced renal function, see the above dosing recommendations for patients with renal impairment.

THE **TREVICTA®** PLAN

The TREVICTA® Plan offers a convenient treatment solution for both you and your patients, monthly XEPLION® and four-per-year (4PY) TREVICTA® [1,5,6]

XEPLION® and TREVICTA® are the two long-acting treatment (LAT) formulations of paliperidone palmitate:



ADMINISTRATIONS PER YEAR

XEPLION® requires once-monthly administration[1]

ADMINISTRATIONS PER YEAR

TREVICTA® requires 3-monthly administration[5]

Patients who are clinically stabilised on treatment with XEPLION® (preferably for 4 months or more) and do not require dose adjustment may be switched to TREVICTA®[5]

TRANSITIONING FROM **XEPLION®** TO **TREVICTA®**[5]

TREVICTA® is indicated for the maintenance treatment of schizophrenia in adult patients who are clinically stable with **XEPLION®**.

- TREVICTA® is administered intramuscularly into either a deltoid or gluteal muscle
- TREVICTA® should be initiated in place of the next scheduled dose of XEPLION® (± 7 days)
- The TREVICTA® dose should be based on the previous 1-monthly XEPLION® dose, using a 3,5-fold higher dose as shown in the following table:

TREVICTA® dose for adults adequately treated with XEPLION®	
If the last XEPLION® dose was:	**Initiate TREVICTA® at the corresponding dose:**
50 mg	175 mg
75 mg	263 mg
100 mg	350 mg
150 mg	525 mg

Following the initial dose, TREVICTA® should be administered once every 3 months (± 2 weeks).[5]

Over time, some patients may require up or down titration of the maintenance dose within the approved 3 monthly dose range of 175 - 525 mg. Due to the long acting properties of TREVICTA®, the response of the patient to an adjusted dose may not be apparent for several months, therefore caution is advised when dose adjustments are to be made.[5]

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HOW DO I **ADMINISTER TREVICTA®?**

Needle selection[5]

Deltoid administration	Gluteal administration
≥90 kg: 22G 1 ½“ (38.1 mm x 0.72 mm) <90 kg: 22G 1“ (25.4 mm x 0.72 mm)	Regardless of weight: 22G 11/2“ (38.1 mm x 0.72 mm)

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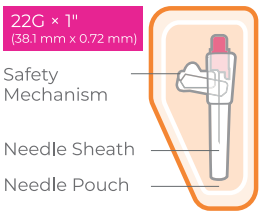
Thin wall safety needles

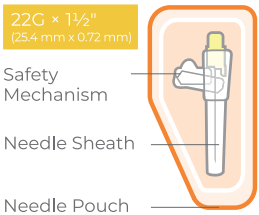
Pink hub

22G × 1"
(38.1 mm x 0.72 mm)



Yellow hub

22G × 1½"
(25.4 mm x 0.72 mm)



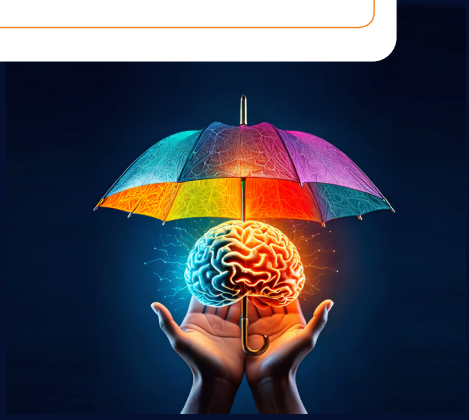
Selecting the appropriate needle[5]

Needle selection is determined by the administration site and patient's weight. Peel off the tabbed label from the syringe and place in the patient's record.
If administering TREVICTA® into a deltoid muscle, the needle size should be selected by patient weight in accordance with the table above.

The thin wall, 22 gauge 1 ½“-inch needle must be used for all gluteal administrations, regardless of body weight.

It is important to only use the needles provided in the TREVICTA® pack. Needles for TREVICTA® should not be substituted.

TREVICTA® does not require any special storage conditions.[5]



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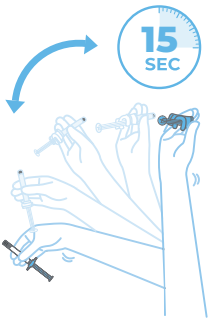


Preparing for administration [5]

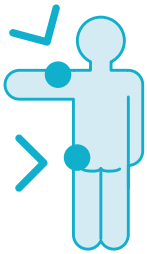
It is important to shake the syringe correctly to ensure a homogeneous suspension:

1. **Position the syringe with the tip pointing upwards**
2. **Vigorously shake with a loose wrist for at least 15 seconds**

If more than 5 minutes pass before administration, shake vigorously again for at least 15 seconds to re-suspend.

The contents of the pre-filled syringe should be visually inspected for foreign matter and discolouration prior to administration.

3



Administering TREVICTA® [5]

TREVICTA® should be administered slowly, and deep into either a deltoid or gluteal muscle, using the entire contents of the syringe in a single administration. Deltoid administration should be into the centre of the muscle, alternating between the two deltoid muscles every three months for each administration.

Gluteal administration should be into the upper-outer quadrant of the muscle, alternating between the two gluteal muscles.

TREVICTA® is intended for intramuscular use only. It must not be administered by any other route. Each dose must only be administered by a healthcare professional, giving the full dose in a single administration.

4

Disposal [5]

Following administration, withdraw the needle and use a thumb or a flat surface to secure the needle in the safety device. The needle is secure when a ‘click’ sound is heard.

The syringe and needle should be disposed of in an approved sharps container.

WHAT IF MY PATIENT **MISSES A DOSE** OF **TREVICTA®?**

TREVICTA® should be administered once every 3 months.[5]

To avoid a missed dose of TREVICTA® patients may be given the injection up to 2 weeks before or after the 3-month time point.[5]

If a dose is missed, clear recommendations are provided with treatment.

If scheduled dose is missed and time since last administration is:	Action:
> 3½ up to 4 months	TREVICTA® should be administered as soon as possible then resume the 3 - monthly administration schedule.
4 to 9 months	Use the recommended re-initiation regimen shown in the table below.
> 9 months	Re-initiate treatment with once-monthly XEPLION® as described on page 4 of this leaflet. TREVICTA® can then be resumed after the patient has been adequately treated with once-monthly XEPLION® preferably for 4 months or more.

Recommended re-initiation regimen after missing 4 to 9 months of TREVICTA®			
If last dose of TREVICTA® was:	Administer 2 XEPLION® doses, 1 week apart (into deltoid muscle)		Then administer TREVICTA® (into deltoid or gluteal muscle)
	Day 1	Day 8	1 month after Day 8
175 mg	50 mg	50 mg	175 mg
263 mg	75 mg	75 mg	263 mg
350 mg	100 mg	100 mg	350 mg
525 mg	100 mg	100 mg	525 mg

HOW DO I TRANSITION TO TREVICTA® IN SPECIAL POPULATIONS?

Patients with renal impairment.[5]

TREVICTA® has not been systematically studied in patients with renal impairment.

For patients with mild renal impairment (creatinine clearance ≥ 50 mL/min to < 80 mL/min), the dose should be adjusted and the patients stabilised using once-monthly XEPLION®, and then transitioned to TREVICTA®.

TREVICTA® is contraindicated in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min).

Patients with hepatic impairment.[5]

TREVICTA® has not been studied in patients with hepatic impairment.

Based on experience with oral paliperidone, no dose adjustment is required in patients with mild or moderate hepatic impairment. However, paliperidone-containing treatments have not been studied in patients with severe hepatic impairment - therefore caution is recommended in these patients.

Elderly patients with schizophrenia.[5]

In general, recommended dosing of TREVICTA® for elderly patients with normal renal function is the same as for younger adult patients with normal renal function.

For elderly patients with reduced renal function, see the above dosing recommendations for patients with renal impairment. Efficacy and safety has not been established in elderly > 65 years.

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TREVICTA® paliperidone palmitate prolonged release suspension for injection

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REFERENCES:

1. XEPLION® Professional Information. January 2022. **2**. Samtani MN, Gopal S, Gassmann-Mayer C, et al. Dosing and switching strategies for paliperidone palmitate. *CNS Drugs* 2011;25(10):1-17. **3.** Taylor D (Ed). Maudsley Prescribing Guidelines in Psychiatry, 11th Edition. Wiley-Blackwell. 2012. **4.** Stahl SM. A Pocket Guide to Atypical Antipsychotics. Dosing, switching and other practical information. C2013. Available from http://schizophrenia.elsevierresource.com/sites/schizophrenia.elsevierresource.com/files/stahl_atypical_antipsychotic_booklet-digital.pdf Accessed 2 September 2016. **5**. TREVICTA® Professional Information Leaflet January 2023 . **6.** Carpiniello B, Pinna F. Critical appraisal of 3 - monthly paliperidone depot injections in the treatment of schizophrenia. *Drug Design, Development and Therapy*. 2016;10:1731-1742.

TREVICTA® PRESCRIBING INFORMATION

S5 TREVICTA® 175 mg, 263 mg, 350 mg, 525 mg prolonged release suspension for injection. 175 mg prolonged release suspension for injection: Each pre-filled syringe contains 273 mg paliperidone palmitate equivalent to 175 mg paliperidone. 263 mg prolonged suspension for injection: Each pre-filled syringe contains 410 mg paliperidone palmitate equivalent to 263 mg paliperidone. 350 mg prolonged release suspension for injection: Each pre-filled syringe contains 546 mg paliperidone palmitate equivalent to 350 mg paliperidone. 525 mg prolonged release suspension for injection: Each pre-filled syringe contains 819 mg paliperidone palmitate equivalent to 525 mg paliperidone. Reg. Nos: 50/2.6.5/0699; 50/2.6.5/0700; 50/2.6.5/0701; 50/2.6.5/0702. For full prescribing information, refer to the latest Professional Information approved by the medicines regulatory authority. January 2023.

XEPLION® PRESCRIBING INFORMATION

S5 XEPLION® 50, 75, 100 or 150mg Prolonged release suspension for intramuscular injection. Each pre-filled syringe contains sterile paliperidone palmitate equivalent to 50, 75, 100 or 150mg of paliperidone respectively. Reg. Nos.:44/2.6.5/0866; 44/2.6.5/0867; 44/2.6.5/0868; 44/2.6.5/0870. For full prescribing information, refer to the latest Professional Information approved by the medicines regulatory authority. January 2022.

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