once-monthly
PERSERIS®
(risperidone) for extended-release injectable suspension
90 mg · 120 mg

IN THE TREATMENT OF SCHIZOPHRENIA IN ADULT PATIENTS, PERSERIS is designed to support patients during pivotal moments in their treatment journey[1,2]

When there's no time to waste, it's time for PERSERIS®

What PERSERIS delivered on Day 1: the first once-monthly risperidone-containing long-acting injectable (LAI)[1,3]

Indivior's proprietary risperidone gel depot delivery system[1,3]

First-in-market risperidone-containing LAI for subcutaneous administration. PERSERIS provided initial peak plasma levels of risperidone in 4 to 6 hours, and continuous delivery throughout the month.

- A direct correlation between the pharmacokinetic profile of PERSERIS and symptom improvement has not been clinically evaluated

No loading dose recommended[1]

- In risperidone-naive patients, establish tolerability with oral risperidone prior to initiating PERSERIS[1]
- Patients who are on stable oral risperidone dosages lower than 3 mg per day or higher than 4 mg per day may not be candidates for PERSERIS[1]
- In patients with renal or hepatic impairment, carefully titrate up to at least 3 mg daily of oral risperidone prior to starting PERSERIS at a dose of 90 mg once monthly[1]
- PERSERIS must be administered by a healthcare provider (HCP)[1]

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. PERSERIS is not approved for the treatment of patients with dementia-related psychosis.

CONTRAINDICATIONS: PERSERIS is contraindicated in patients with a known hypersensitivity to risperidone, its metabolite, paliperidone, or to any of its components. Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been reported in patients treated with risperidone or paliperidone.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including BOXED WARNING.

Choose PERSERIS®: the first once-monthly risperidone-containing LAI for adults with schizophrenia[1,3]

PERSERIS is designed to support your patients during pivotal moments in their treatment journey[1,4]

Indivior's proprietary risperidone gel depot delivery system

Delivered initial peak risperidone plasma levels in 4 to 6 hours of the first dose, followed by a sustained release of risperidone throughout the month[1,3]*

- A direct correlation between the pharmacokinetic profile of PERSERIS and symptom improvement has not been clinically evaluated

Systemic safety profile

Consistent with the known safety profile of oral risperidone, with no new safety signals reported in an open-label 12-month extension study[5,6]

Straightforward dosing

One injection, once a month. Two dosage strengths to choose from[1]

Select dosing considerations

- In risperidone-naive patients, establish tolerability with oral risperidone prior to initiating PERSERIS[1]
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*By the end of the second month, steady-state plasma concentrations were reached and maintained for 4 weeks.[3]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Cerebrovascular Adverse Reactions: In trials of elderly patients with dementia-related psychosis, there was a significantly higher incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, in patients treated with oral risperidone compared to placebo. PERSERIS is not approved for use in patients with dementia-related psychosis.

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Neuroleptic Malignant Syndrome (NMS), a potentially fatal symptom complex, has been reported with antipsychotic medications. Clinical manifestations include hyperpyrexia, muscle rigidity, altered mental status including delirium, and autonomic instability (see full Prescribing Information). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. If NMS is suspected, immediately discontinue PERSERIS and provide symptomatic treatment and monitoring.

Tardive Dyskinesia (TD) may develop in patients treated with antipsychotic drugs. The risk of developing TD and likelihood that it will become irreversible are believed to increase with treatment duration and total cumulative dose. TD can develop after relatively brief treatment periods even at low doses, or after treatment discontinuation. Elderly patients, especially elderly women, appear to be at increased risk, but it is impossible to predict which patients will develop TD. Therefore, PERSERIS should be prescribed in a manner that is most likely to minimize the occurrence of TD. Discontinue treatment if clinically appropriate.

Metabolic Changes that may increase cardiovascular/cerebrovascular risk, have been associated with atypical antipsychotics (APs).

- **Hyperglycemia and Diabetes Mellitus (DM),** in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, have been reported in patients treated with APs, including risperidone. Patients with DM who are started on atypical APs, including PERSERIS, should be monitored regularly for worsening of glucose control. Patients at risk for DM (e.g., obesity, family history of diabetes) who are starting treatment with atypical APs, including PERSERIS, should undergo fasting blood glucose (FBG) testing at the beginning of treatment and periodically while treated. Any patient treated with atypical APs, including PERSERIS, should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical APs, including PERSERIS, should undergo FBG testing. In some cases, hyperglycemia has resolved when risperidone was discontinued; however, some patients required continuation of antidiabetic treatment despite discontinuation of risperidone.
- **Dyslipidemia** has been observed in patients treated with atypical APs. When initiating PERSERIS, obtain a fasting lipid profile and monitor periodically during treatment.
- **Weight Gain** has been observed with atypical AP use. Monitoring weight is recommended.

Hyperprolactinemia: Risperidone elevates prolactin levels, and the elevation persists during chronic administration. Risperidone is associated with higher levels of prolactin elevation than other antipsychotic agents. Hyperprolactinemia may inhibit reproductive function in female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating drugs. Long-standing hyperprolactinemia, when associated with hypogonadism, may lead to decreased bone density in females and males.

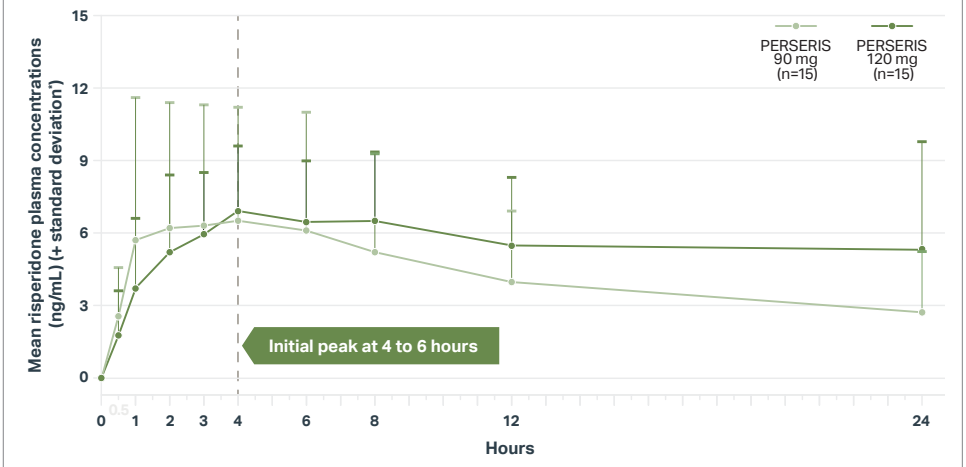
Orthostatic Hypotension and Syncope: Risperidone may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, particularly at treatment initiation, re-initiation, or dose increase. Use with particular caution in patients with known cardiovascular disease, cerebrovascular disease, and conditions which predispose patients to hypotension, and in the elderly and patients with renal or hepatic impairment. Monitor such patients and consider a dose reduction if hypotension occurs.

Falls: Somnolence, postural hypotension, motor instability, and sensory instability have been reported with the use of antipsychotics, including PERSERIS, which may lead to falls, and consequently, fractures or other fall-related injuries. Assess the risk of falls when initiating treatment and recurrently during treatment.

PERSERIS® delivers peak levels of risperidone after the first dose[1]

Patients achieved initial peak plasma levels of risperidone in 4 to 6 hours after starting treatment[1]

Risperidone concentrations within 24 hours[1,5]



*Standard deviations are expressed as one-sided bars for visual clarity.

A direct correlation between the pharmacokinetic profile of PERSERIS and symptom improvement has not been clinically evaluated.

- At 10-14 days after injection, patients taking PERSERIS experienced a second peak in plasma levels of risperidone[1]

Study description: A Phase I, open-label, single-center, single ascending dose study of the safety, tolerability, and pharmacokinetic profile over 85 days of PERSERIS (90 mg and 120 mg) in 30 patients with clinically stable schizophrenia who were not taking risperidone.[5]

Day 1 with PERSERIS

In hours of the first injection, initial peak plasma levels of risperidone were reached[1]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Leukopenia, Neutropenia, and Agranulocytosis have been reported with antipsychotic agents, including risperidone. In patients with history of clinically significant low white blood count (WBC) or absolute neutrophil count (ANC), or history of drug-induced leukopenia or neutropenia, perform a complete blood count frequently during the first few months of therapy. Consider discontinuation at the first sign of clinically significant decline in WBC in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms/signs of infection; treat promptly if such symptoms/signs occur. Discontinue PERSERIS in patients with ANC <1000/mm^3 and follow WBC until recovery.

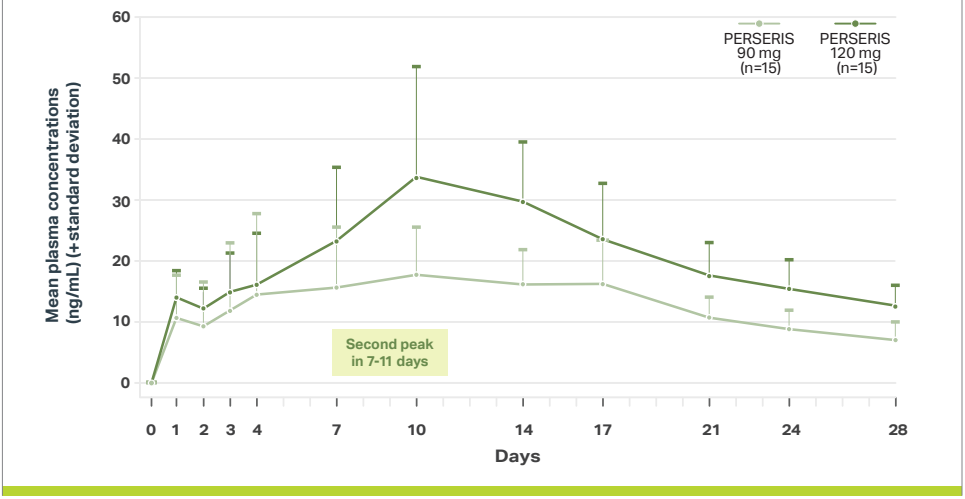
Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including BOXED WARNING.

After the first injection, PERSERIS® reached clinically relevant levels[1,5]

A second peak in total active moiety* was reached in 7 to 11 days[1,3]

The first peak was reached in 4-48 hours.[1,3]

Total active moiety concentrations over 1 month[1,5]



*Total active moiety refers to the combined concentrations of risperidone and paliperidone.[1]

- Total active moiety plasma concentrations approached steady-state levels after the first injection[1]
- By the end of month 2, steady-state plasma concentrations were reached and maintained for 4 weeks[3]

Continuous risperidone delivery after each injection

PERSERIS was designed to deliver sustained plasma levels of risperidone throughout the month[1,5]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Potential for Cognitive and Motor Impairment: Antipsychotics including PERSERIS may cause somnolence and impair judgment, thinking, and motor skills. Caution patients about operating machinery, including motor vehicles, until they are reasonably certain PERSERIS does not affect them adversely.

Seizures were observed in risperidone studies in adults with schizophrenia. PERSERIS should be used cautiously in patients with a history of seizures or other conditions that potentially lower the seizure threshold.

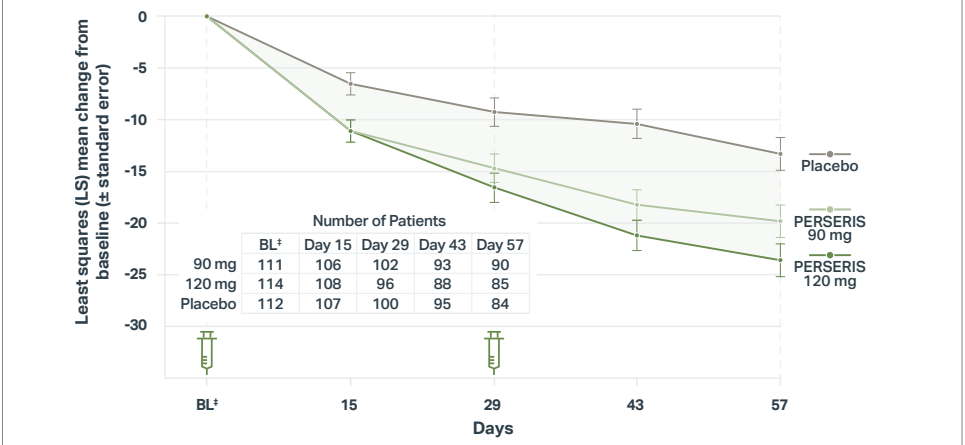
Dysphagia: Esophageal dysmotility and aspiration can occur. Use cautiously in patients at risk for aspiration.

Priapism has been reported with other risperidone products. Severe priapism may require surgical intervention.

PERSERIS® may help establish and maintain symptom control[1,4]

For patients experiencing acute exacerbations, PERSERIS delivered statistically significant improvements from baseline in PANSS* total scores vs placebo for both doses at Day 57[1,4]

Change in PANSS total scores[1,5†]



*PANSS=Positive and Negative Syndrome Scale.
†*P*=0.007 and *P*<0.0001 vs placebo for 90 mg and 120 mg PERSERIS, respectively, at Day 57.[7]
‡BL=baseline.

Study description: An 8-week, Phase III, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of PERSERIS (90 mg and 120 mg) compared with placebo in 354 inpatients.[1]

The average change in PANSS total scores from baseline at the end of the study was -13.37 for placebo, -19.86 for 90 mg of PERSERIS, and -23.61 for 120 mg of PERSERIS.[1]

Primary Endpoint

- Statistically significant PANSS total score reductions from baseline were shown vs placebo for both doses of PERSERIS at Day 57[1,5]
- The study was not designed to evaluate differences between PERSERIS dosage strengths[1,5]

May help maintain symptom control

For patients experiencing acute exacerbations, PERSERIS may help them gain and maintain control of symptoms[1]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Body Temperature Regulation: Atypical antipsychotics may disrupt the body's ability to reduce core body temperature. Use with caution during strenuous exercise, exposure to extreme heat, dehydration, or when taking anticholinergic medications.

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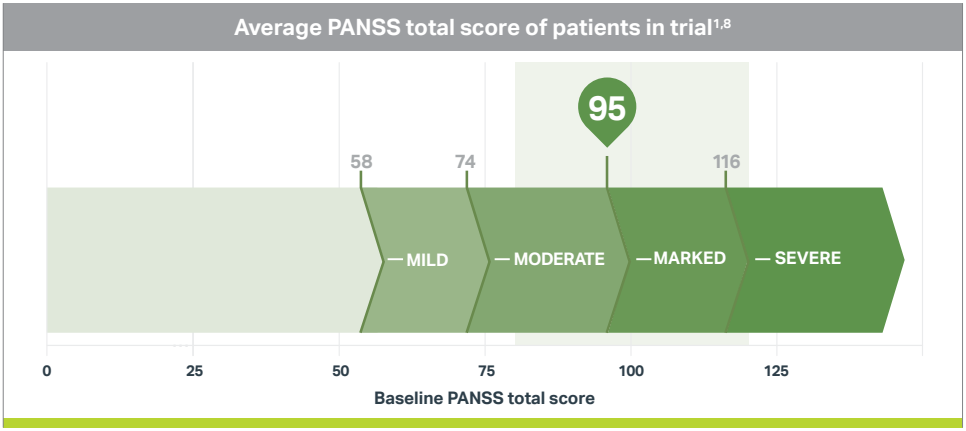
Adult patients experiencing acute exacerbations of schizophrenia were evaluated[1]



Study description: An 8-week, Phase III, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of PERSERIS (90 mg and 120 mg) compared with placebo in 354 inpatients.[1]

Selected inclusion criteria

- Patients aged 18 to 55 years (mean: 40 to 43 years)[1]
- Adult patients experiencing acute exacerbations of schizophrenia[1]
- Patients with PANSS total scores from 80 to 120[1]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

ADVERSE REACTIONS: The most common adverse reactions in a clinical trial (≥ 5% and greater than placebo) were increased weight, constipation, sedation/somnolence, pain in extremity, back pain, akathisia, anxiety, and musculoskeletal pain. The most common injection site reactions (≥ 5%) were injection site pain and erythema. This is not a complete list of potential adverse events. Please see the full Prescribing Information for a complete list.

DRUG INTERACTIONS

- Carbamazepine and other strong CYP3A4 inducers decrease risperidone plasma concentration.
- Fluoxetine, paroxetine, and other strong CYP2D6 inhibitors increase risperidone plasma concentration.
- Use with other CNS drugs or alcohol may increase nervous system disorders.
- PERSERIS may enhance hypotensive effects of hypotensive agents.
- PERSERIS may antagonize the pharmacologic effects of dopamine agonists.
- Dosage change in PERSERIS or methylphenidate may increase risk of extrapyramidal symptoms.

USE IN SPECIFIC POPULATIONS

Pregnancy: PERSERIS may cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. Advise patients to notify their healthcare professional if they become or intend to become pregnant during treatment with PERSERIS. Patients exposed to PERSERIS during pregnancy may be registered with the National Pregnancy Registry for Atypical Antipsychotics (**1-866-961-2388** or **http://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/**).

Lactation: Infants exposed to risperidone through breastmilk should be monitored for excess sedation, failure to thrive, jitteriness, and extrapyramidal symptoms.

The systemic safety profile of PERSERIS® was consistent with the known safety profile of oral risperidone[1]

The safety and tolerability of PERSERIS were studied in a Phase III, 8-week, randomized, double-blind, placebo-controlled clinical study.[1,5]

Adverse drug reactions (ADRs) occurring in ≥5% of patients[1]			
ADRs	**90 mg (n=115) %**	**120 mg (n=117) %**	**Placebo (n=118) %**
Weight increased	13	13	3
Constipation	7	8	5
Sedation/somnolence	7	8	0
Pain in extremity	1	8	5
Anxiety	3	7	5
Back pain	4	7	4
Akathisia	3	7	4
Musculoskeletal pain	5	5	3

- A typical increase in mean prolactin levels was observed for both doses of PERSERIS from baseline to end of study; mean prolactin for the placebo group remained stable during the study[1]
- Extrapyramidal symptom (EPS)-related ADRs ≥2% were akathisia (90 mg: 3%; 120 mg: 7%; placebo: 4%), extrapyramidal disorder (90 mg: 4%; 120 mg: 2%; placebo: 1%), and dystonia (90 mg: 0%; 120 mg: 1%; placebo: 3%)[1]
- There was no single adverse reaction leading to discontinuation that occurred at a rate of ≥2% (and greater than placebo) in patients treated with PERSERIS[1]
- The mean change in weights of patients taking PERSERIS 90 mg or 120 mg increased ~10 lbs (4.4 kg) and ~12 lbs (5.3 kg), respectively, from baseline to Day 57; mean weight of patients in the placebo arm increased ~6 lbs (2.6 kg)[1]
  - Weight gain ≥7% from baseline occurred in 33% of patients in the 90-mg group, 42% in the 120-mg group, and 18% in the placebo group[1]

References: 1. PERSERIS [prescribing information]. North Chesterfield, VA: Indivior Inc. **2.** Pietrini F, Albert U, Ballerini A, et al. *Neuropsychiatric Disease and Treatment.* 2019;15:1045-1060. **3.** Tchobaniouk LV, McAllister EE, Bishop DL, et al. *Patient Prefer Adherence.* 2019;13:2233-2241. **4.** Ivaturi V, Gopalakrishnan M, Gobburu JVS, et al. *Br J Clin Pharmacol.* 2017;83(7):1476-1498. **5.** Data on file. Indivior Inc. North Chesterfield, VA. **6.** Andorn A, Graham J, Csernansky J, et al. *J Clin Psychopharmacol.* 2019;39(5): 428-533. **7.** Le Moigne A, Fava M, Csernansky J, et al. *J Clin Psychopharmacol.* 2021;41(1):76-77. **8.** Leucht S, Kane JM, Kissling W, Hamann J, Etschel E, Engel RR. *Schizophr Res.* 2005;79(2-3):231-238.

IMPORTANT SAFETY INFORMATION

USE IN SPECIFIC POPULATIONS (CONT'D)

Pediatric Use: Safety and effectiveness of PERSERIS have not been established in pediatric patients.

Renal or Hepatic Impairment: Carefully titrate on oral risperidone up to at least 3 mg before initiating treatment with PERSERIS at a dose of 90 mg.

Patients with Parkinson's Disease or dementia with Lewy Bodies can experience increased sensitivity to risperidone. Manifestations can include confusion, obtundation, postural instability with frequent falls, extrapyramidal symptoms, and clinical features consistent with NMS.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including BOXED WARNING.

Systemic safety profile remained consistent with the known safety profile of oral risperidone over the course of a year[1,5,6]

No new safety signals were reported in a 12-month open-label Phase III extension study (N=500) following an 8-week pivotal study that evaluated the safety and tolerability of PERSERIS.[5,6]

Treatment-emergent adverse events (TEAEs) occurring in ≥5% of all patients[5]	
TEAEs	**All patients (N=500) %**
Weight increased	13
Schizophrenia	8
Insomnia	7
Akathisia	6
Upper respiratory tract infection	5
Headache	5

- Mean weight of all patients receiving PERSERIS increased ~4 lbs (~2 kg) from baseline to Day 85, then remained stable for the remainder of the study[1]
- Overall, 11.6% of patients experienced TEAEs leading to study discontinuation[5]
- The most frequently occurring TEAEs leading to study discontinuation were schizophrenia (2.0%), weight increased (0.8%), and akathisia (0.8%)[5]
- The most commonly reported ADRs associated with EPS for all patients were akathisia (6%), tremor (2%), and extrapyramidal disorder (2%)[5]

Less than 1% of patients discontinued due to weight gain[5]

The most commonly reported ADRs leading to discontinuation[5]	
ADRs	**All patients (N=500) %**
Weight increased	1
Akathisia	1
Sedation/somnolence	1
Tremor	1
Galactorrhea	1

- No serious adverse events were attributed to PERSERIS[5]
- There were no trends in vital signs, electrocardiogram (ECG) parameters, extrapyramidal symptoms, or suicidality that were considered clinically important[5,6]

IMPORTANT SAFETY INFORMATION

USE IN SPECIFIC POPULATIONS (CONT'D)

To report a pregnancy or side effects associated with taking PERSERIS or any safety related information, product complaint, request for medical information, or product query, please contact PatientSafetyNA@indivior.com or 1-877-782-6966.

See accompanying full Prescribing Information including BOXED WARNING; for more information about PERSERIS visit www.perserishcp.com.

Support your patients during pivotal moments in their treatment journey

Choose PERSERIS®: the first once-monthly risperidone-containing LAI[1,3]

In that pivotal moment when your patient needs an LAI, consider PERSERIS first

Indivior's proprietary risperidone gel depot delivery system

Delivered initial peak risperidone plasma levels in 4 to 6 hours of the first dose, followed by a sustained release of risperidone throughout the month[1,3]*

- A direct correlation between the pharmacokinetic profile of PERSERIS and symptom improvement has not been clinically evaluated

Systemic safety profile

Consistent with the known safety profile of oral risperidone, with no new safety signals reported in an open-label 12-month extension study[5,6]

Straightforward dosing

One injection, once a month. Two dosage strengths to choose from[1]

Select dosing considerations

- In risperidone-naive patients, establish tolerability with oral risperidone prior to initiating PERSERIS[1]
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INDIVIOR®

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PERSERIS®
(risperidone) for extended-release injectable suspension
90 mg · 120 mg

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