

PERSERIS® (risperidone) for extended-release injectable suspension, for subcutaneous use: Medical Affairs Product Fact Sheet

Indications and Usage¹

PERSERIS is indicated for the treatment of schizophrenia in adults.

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 and has not been studied in this population.

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.

Adverse Reactions¹

The most common adverse reactions in clinical trials ($\geq 5\%$ and greater than twice placebo) were increased weight, sedation/somnolence, and musculoskeletal pain.

Additional Important Safety Information is provided later in this document. See accompanying full Prescribing Information, including BOXED WARNING, that is included with this document.

Dosage Forms and Strengths¹

For extended-release injectable suspension: 90 mg and 120 mg risperidone.

Dosage and Administration¹

- PERSERIS is to be administered as an abdominal subcutaneous injection only. Do not administer by any other route.
- Each injection must be administered by a healthcare professional using the prepackaged injection syringe and enclosed safety needle.
- For patients who have never taken risperidone, establish tolerability with oral risperidone prior to starting PERSERIS.
- Initiate PERSERIS at a dose of 90 mg or 120 mg once monthly by subcutaneous injection. Do not administer more than one dose (90 mg or 120 mg total) per month.
- Based on average plasma concentrations (C_{avg}) of risperidone and total active moiety, 90 mg PERSERIS corresponds to 3 mg/day oral risperidone and 120 mg PERSERIS corresponds to 4 mg/day oral risperidone.
- PERSERIS is not recommended for patients who are on stable oral risperidone doses lower than 3 mg/day or higher than 4 mg/day.
- Neither a loading dose nor any supplemental oral risperidone is recommended. A patient who misses a dose should receive the next dose as soon as possible.

How Supplied/Storage and Handling¹

How Supplied

PERSERIS (risperidone) for extended-release injectable suspension, for subcutaneous use is, when fully mixed, a viscous suspension that varies from white to yellow-green and is available in dosage strengths of 90 mg and 120 mg.

PERSERIS 90 mg is supplied in a single-dose kit, packaged in a carton (NDC 12496-0090-1), containing the following:

- One pouch with a sterile syringe (labelled 'P') prefilled with risperidone powder
- One pouch with a sterile syringe (labelled 'L') prefilled with the delivery system, and desiccant.
- One 18-gauge, 5/8-inch sterile safety needle.

PERSERIS 120 mg is supplied in a single-dose kit, packaged in a carton (NDC 12496-0120-1), containing the following:

- One pouch with a sterile syringe (labelled 'P') prefilled with risperidone powder.
- One pouch with a sterile syringe (labelled 'L') prefilled with the delivery system, and desiccant.
- One 18-gauge, 5/8-inch sterile safety needle.

Storage and Handling

Store in refrigerator at 2° to 8°C (36° to 46°F). Allow PERSERIS kit to come to room temperature, 20°C to 25°C (68°F to 77°F), for at least 15 minutes prior to mixing.

PERSERIS may be stored in its unopened original packaging at room temperature, 20°C to 25°C (68°F to 77°F), for up to 7 days prior to administration. After removal from the refrigerator, use PERSERIS within 7 days or discard.

Instructions for Use

Important Information

- For abdominal subcutaneous injection, only. Do not administer by any other route.
- To be administered by a healthcare professional only.
- Please read the instructions carefully before handling this product.
- Allow package to come to room temperature for at least 15 minutes prior to preparation.
- Only prepare medication when you are ready to administer the dose.
- As a universal precaution, always wear gloves.

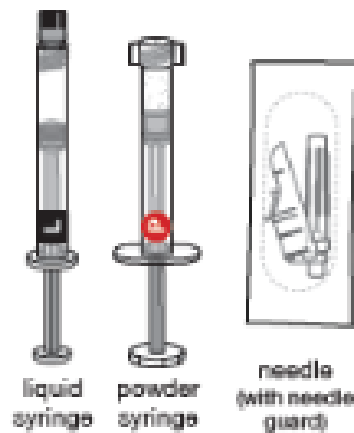
1 CHECK CONTENTS

See Figure 1

- One Liquid Syringe (L) prefilled with the delivery system. Inspect liquid solution for foreign particles. This is the syringe you will use to inject the patient.
- One Powder Syringe (P) prefilled with Risperidone powder. Inspect syringe for consistency of powder color and for foreign particles.
- One sterile 18-gauge, 5/8-inch safety needle.
-

Parenteral drug products should always be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit

Figure 1

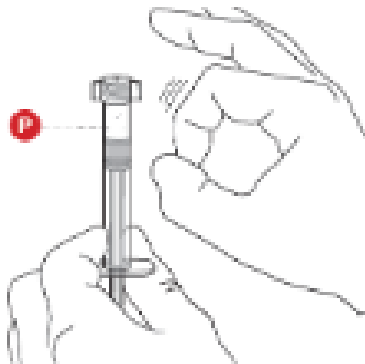


2 TAP POWDER SYRINGE

See Figure 2

Hold the Powder Syringe upright and tap the barrel of the syringe to dislodge the packed powder. NOTE: Powder can become packed during shipping.

Figure 2

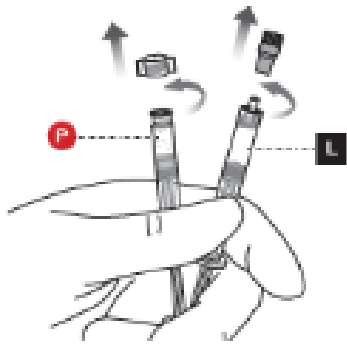


3 UNCAP LIQUID AND POWDER SYRINGES

See Figure 3

Remove the cap from the Liquid Syringe, then remove the cap from the Powder Syringe. Holding both syringes in your non-dominant hand can help with this step.

Figure 3

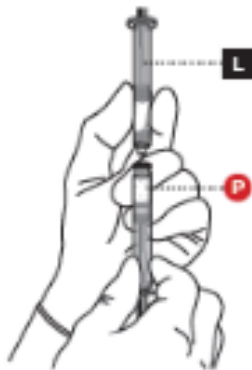


4 CONNECT THE SYRINGES

See Figure 4

Place the Liquid Syringe on top of the Powder Syringe (to prevent powder spillage) and connect the syringes by twisting approximately $\frac{3}{4}$ turn. Do not over tighten. Keep your fingers off the plungers during this step to avoid spillage of the medication.

Figure 4

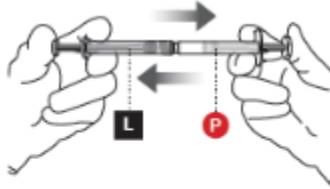


5 MIX THE PRODUCT

See Figure 5

Failure to fully mix the medication could result in incorrect dosage.

Figure 5



Premixing

- Transfer the contents of the Liquid Syringe into the Powder Syringe.
- Gently push the Powder Syringe plunger until you feel resistance (to wet powder and avoid compacting).
- Repeat this gentle back-and-forth process for 5 cycles.

Complete mixing

- Continue mixing the syringes for an additional 55 cycles.
- This mixing can be more vigorous than when premixing.
- Figure 5 illustrates a correct full cycle.

When fully mixed, the product should be a cloudy suspension that is uniform in color. It can vary from white to yellow-green in color. If you see any clear areas in the mixture, continue to mix until the distribution of the color is uniform. The product is designed to deliver risperidone 90 mg or 120 mg.

6 PREPARE INJECTION SYRINGE

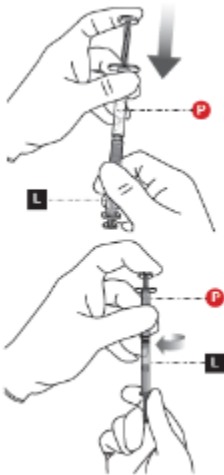
See Figure 6

Failure to aspirate the liquid from the Powder Syringe may result in incorrect dosage.

- First, transfer all contents into the Liquid Syringe.
- Next, perform the following actions SIMULTANEOUSLY:
 - maintain slight pressure on the Powder Syringe plunger and
 - pull back gently on the Liquid Syringe plunger while twisting the syringes apart.
- Finally, attach the safety needle by twisting until finger tight.

Check that medication is uniform in color and free from foreign particles.

Figure 6

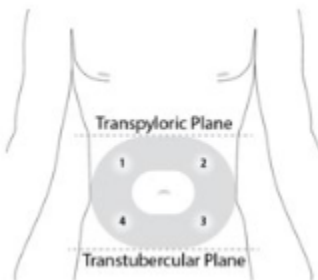


7 PREPARE THE ABDOMINAL INJECTION SITE

See Figure 7

Choose an injection site on the abdomen with adequate subcutaneous tissue that is free of skin conditions (e.g., nodules, lesions, excessive pigment). It is recommended that the patient is in the supine position. Do not inject into an area where the skin is irritated, reddened, bruised, infected or scarred in any way. Clean the injection site well with an alcohol pad. To help minimize irritation, rotate injection sites following a pattern similar to the illustration (Figure 7).

Figure 7

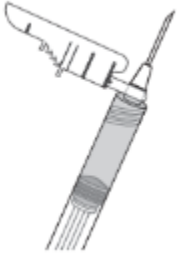


8 REMOVE EXCESS AIR FROM SYRINGE

See Figure 8

Hold the syringe upright for several seconds to allow air bubbles to rise. Remove needle cover and slowly depress the plunger to push out the excess air from the syringe. If medication is seen at the needle tip, pull back slightly on the plunger to prevent medication spillage. Due to the viscous nature of the medication, bubbles will not rise as quickly as those in an aqueous solution.

Figure 8



9 PINCH INJECTION SITE

See Figure 9

Pinch the skin around the injection area. Be sure to pinch enough skin to accommodate the size of the needle. Lift the adipose tissue from the underlying muscle to prevent accidental intramuscular injection.

Figure 9



10 INJECT THE MEDICATION

See Figure 10

Insert needle fully into the subcutaneous tissue. Inject the medication slow and steady. PERSERIS is for subcutaneous administration only. Do not inject by any other route. NOTE: Actual angle of injection will depend on the amount of subcutaneous tissue.

Figure 10



11 WITHDRAW NEEDLE

See Figure 11

Withdraw the needle at the same angle used for insertion and release pinched skin. Do not rub the injection area after the injection. If there is bleeding, apply a gauze pad or bandage but use minimal pressure.

Figure 11



12 LOCK THE NEEDLE GUARD AND DISPOSE OF SYRINGE

See Figure 12

Lock the needle guard into place by pushing it against a hard surface such as a table. Dispose of all syringe components in a secure sharps disposal container.

Figure 12



13 INSTRUCT THE PATIENT

See Figure 13

Advise the patient that they may have a lump for several weeks that will decrease in size over time. It is important that the patient not rub or massage the injection site and to be aware of the placement of any belts or clothing waistbands.

Figure 13



Please see the accompanying Prescribing Information for more information.

ABBREVIATED PHASE 2A CLINICAL TRIAL INFORMATION

Phase 2a Pharmacokinetic Study Information: Multiple Ascending Dose (MAD), Open-Label Study to Assess the Safety, Tolerability, Pharmacokinetics of 60 mg, 90 mg and 120 mg RBP-7000 (PERSERIS) (RB-US-09-0009)²

- The phase 2A, open-label, multiple ascending dose study included 45 subjects with clinically stable schizophrenia and was designed to evaluate the pharmacokinetic profile of risperidone, 9-hydroxyrisperidone, and total active risperidone (risperidone and 9-hydroxyrisperidone) after multiple monthly subcutaneous (SC) injections of 60 mg, 90 mg, and 120 mg of PERSERIS (risperidone using the ATRIGEL[®] delivery system) in subjects on a stable oral risperidone dose of 2 mg, 3 mg, or 4 mg, respectively.
- Treatment consisted of 3 once monthly SC injections of PERSERIS on Day 1, Day 29, and Day 57. Multiple blood samples for risperidone, 9-hydroxyrisperidone, and total active risperidone pharmacokinetic assessments were collected after each SC injection of PERSERIS.

Results included:

- Plasma concentrations for risperidone, 9-hydroxyrisperidone, and total active risperidone reached an initial T_{max} at 4 to 6 hours and nearly reached steady state after the first subcutaneous injection of PERSERIS at all 3 dose levels
- Steady state was attained by Day 29 for risperidone and by Day 57 for 9-hydroxyrisperidone and total active risperidone
- Neither loading doses of PERSERIS nor supplemental doses of oral risperidone were included in this study

Citation: Laffont CM, Gomeni R, Zheng B, et al. Population pharmacokinetics and prediction of dopamine D2 receptor occupancy after multiple doses of RBP- 7000, a new sustained-release formulation of risperidone, in schizophrenia patients on stable oral risperidone treatment. *Clin Pharmacokinet.* 2014;53;533-543

ABBREVIATED PHASE 3 CLINICAL TRIAL INFORMATION

A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of PERSERIS (90 mg and 120 mg) as a Treatment in Subjects with Acute Schizophrenia Over 8 Weeks (2 Subcutaneous Doses) (RB-US-09-0010)⁴

Study Objectives:

- Primary Efficacy: Change in the Positive and Negative Syndrome Scale (PANSS) total score from baseline to the end of the study (Day 57)
- Secondary Efficacy: Change in the Clinical Global Impressions Severity (CGI-S) scale from baseline to the end of the study

Select Inclusion Criteria:

- Adult men and women between the ages of 18 and 55 years
- Diagnosis of schizophrenia per the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-IV-TR)*
- Currently in an acute exacerbation that occurred 8 weeks or less before the screening visit and would have benefited from psychiatric hospitalization or continued hospitalization
- At screening, a PANSS total score of 80–120, and a score of greater than 4 on at least 2 of the following 4 items: hallucinatory behavior, delusions, conceptual disorganization, or suspiciousness/persecution.
- The subjects were on average 41 years old, 73% black, 24% white, and 1% Asian, with a mean BMI of 29.9 kg/m². The mean duration of treatment was 47.1 days and 84.6% of subjects were compliant with the study drug. (5)

Select Exclusion Criteria:

- Patients who had an improvement in the PANSS total score of $\geq 20\%$ between initial screening and the first injection
- Treatment at any time with clozapine for treatment-resistant schizophrenia
- Diagnosis of substance dependence, with the exception of nicotine or caffeine, before screening per *DSM-IV-TR*

Study Methods:

- Tolerability and acute hypersensitivity to oral risperidone was assessed for all study participants at the screening visit for at least 2 doses given 24 hours apart
- Eligible participants were placed into an inpatient setting, if not already an inpatient, and tapered off their current oral antipsychotic if applicable
- Eligible participants were randomized to receive 2 doses, 28 days apart, of PERSERIS 90 mg or 120 mg or “placebo”
- No supplemental oral risperidone was permitted during the study.

Statistical Analysis: The primary and secondary efficacy endpoints were assessed using a mixed-effects model with repeated measures (MMRM), reporting least-squares mean (LS mean), standard error, 95% confidence interval, and *P*-values

Study Results

A statistically significant improvement was observed for the primary endpoint of reduction in PANSS total scores from baseline to end of study for PERSERIS 90 mg and 120 mg when compared to “placebo.” A statistically significant improvement was observed for the secondary endpoint of reduction in CGI-S from baseline to end of study for PERSERIS 90 mg and 120 mg when compared to “placebo.”

Primary Efficacy:

- The LS means from the repeated-measures analysis for the change from baseline in the PANSS total scores for placebo was -9.219 (SE, 1.2162).
- On the basis of the repeated-measures analysis, subjects who received 90 or 120 mg of PERSERIS showed significant improvement in the difference from baseline in PANSS total scores at the end of the study compared with placebo during the duration of the study (90-mg PERSERIS, -6.148 [-9.982 to -2.314], $P = 0.0004$; 120-mg PERSERIS, -7.237 [-11.045 to -3.429], $P < 0.0001$)

Secondary Efficacy: Subjects who received 90- or 120-mg PERSERIS showed significant improvement by the repeated-measures analysis in the LS mean changes from baseline through the end of the study in CGI-S scores compared with placebo during the duration of the study (90-mg PERSERIS, -0.350 [-0.557 to -0.143], $P = 0.0002$; 120-mg PERSERIS, -0.396 [-0.602 to -0.190], $P < 0.0001$).

Adverse Effects: The most common adverse events were headache (23.7% for placebo vs 15.4% and 17.4% for 90- and 120-mg PERSERIS, respectively), injection site pain (19.5% for placebo vs 15.7% and 22.2% for 90- and 120-mg PERSERIS, respectively), and weight gain (3.4% for placebo vs 13.0% and 12.8% for 90- and 120-mg PERSERIS, respectively). (4)

Citation: Nasser AF, Henderson DC, Fava M, et al. Efficacy, safety, and tolerability of PERSERIS (PERSERIS) once-monthly risperidone for the treatment of acute schizophrenia: an 8-week, randomized, double-blind, placebo-controlled, multicenter phase 3 study. *J Clin Psychopharmacol.* 2016;36(2):130-140

Abbreviated Phase 3 Clinical Trial Information: An Open-Label, Long-Term Safety and Tolerability Study of PERSERIS in the Treatment of Subjects with Schizophrenia (RB-US-03-0005)⁶

Study Objectives:

- Primary Efficacy: Assess the long-term safety and tolerability of PERSERIS SC injections in subjects with schizophrenia
- Secondary Efficacy: Continue collecting clinical outcome data with PERSERIS SC injections in subjects with schizophrenia using the PANSS and CGI-S scale

Select Inclusion Criteria:

De Novo Subjects

- Adult men and women between the ages of 18 and 65 years
- Diagnosis of schizophrenia per the *DSM-IV-TR*
- A total PANSS total of ≤ 70 at the time of screening
- Otherwise healthy on the basis of physical examination
- Provided written informed consent Rollover Subjects
- Provided written informed consent
- Were considered eligible to enroll based on completion of EOS (Day 57 of Study RB-US-09-0010) assessments and the medical judgment of the Investigator

Select Exclusion Criteria:

- De Novo Subjects: Subjects taking daily oral risperidone at a dose ≥ 6 mg/day, subject who had received a LAI antipsychotic within 120 days of study screening
- Rollover Subjects: Subjects requiring an inpatient treatment setting at the end of Study RB-US-09-0010 or developed an unstable medical condition during Study RB-US-09-0010

Study Methods:

- All subjects returned to the study site every 14 days (± 2 days) for the first 4 injections from Visit 6 through Visit 12, and then every 28 days ($+5$ days) from Visit 13 through the end of the open-label treatment phase
- All subjects were assigned to receive treatment with 120 mg PERSERIS, which was subject to a 1-time taper for tolerability to the 90-mg dose at the Investigator's discretion. All subjects could have been up-titrated again to 120 mg at the investigator's discretion.

Statistical Analysis: Change from baseline for each score was summarized by visit using descriptive statistics. For all scores, if one or more of the items was missing, then the score was set to missing. No imputation was conducted for missing/incomplete PANSS or CGI-S assessments. The analysis of efficacy was based on the Safety Analysis Set.

Study Results

Primary Efficacy:

- Overall, 73.4% of subjects had 1 or more TEAE during the study and 54.0% of subjects had TEAEs assessed by the Investigator as related to study drug.
- There were 34 (6.8%) subjects with SAEs; however, none were assessed by the Investigator as related to study. Four of these subjects (0.8%) had serious TEAEs leading to death, including cardiac arrest, psychotic disorder, pulmonary embolism, and death (cause unknown at the time of study conclusion).
- Fifty-eight subjects (11.6%) had TEAEs leading to study discontinuation and 43 subjects (8.6%) had TEAEs leading to dose modification

Secondary Efficacy:

- Among de novo subjects, the PANSS total scores remained stable throughout the study with mean (\pm SD) values of 58.0 (± 8.33) at baseline and 57.3 (± 10.09) at EOS. Among rollover subjects, the PANSS total

scores decreased (improved) throughout the study, with changes from baseline at EOS ranging from 10.9 (rollover PERSERIS 120 mg) to -20.2 (rollover placebo)

- The CGI-S scores remained stable throughout the study with mean (\pm SD) values of 3.4 (\pm 0.71) at baseline and 3.2 (\pm 0.69) at end of study (Table 14.2.2) for all subjects combined.

Adverse Effects: The most frequently reported adverse effects in all subjects were injection site pain and weight increased, occurring in 13.0% and 12.8% of subjects, respectively. Treatment-emergent AEs occurring in \geq 5.0% to 10% of subjects were schizophrenia, insomnia, injection site nodule, akathisia, injection site induration, upper respiratory tract infection, and headache.

Citation: Andorn, Ann, Graham, Jay; Csernansky, John, et al. Monthly Extended-Release Risperidone (PERSERIS) in the Treatment of Schizophrenia, *J Clin Psychopharmacol*: Sept-Oct 2019, Vol, Issue 5, p 428-43.

References

1. PERSERIS (risperidone) for extended-release injectable suspension, for subcutaneous use, Prescribing Information. North Chesterfield, VA: INDIVIOR, Inc.; December 2019.
2. Laffont CM, Gomeni R, Zheng B, et al. Population pharmacokinetics and prediction of dopamine D2 receptor occupancy after multiple doses of RBP- 7000, a new sustained-release formulation of risperidone, in schizophrenia patients on stable oral risperidone treatment. *Clin Pharmacokinet*. 2014;53;533-543.
3. Data on File: RB-US-09- 0009. Indivior Inc.
4. Nasser AF, Henderson DC, Fava M, et al. Efficacy, safety, and tolerability of PERSERIS once-monthly risperidone for the treatment of acute schizophrenia: an 8-week, randomized, double-blind, placebo-controlled, multicenter phase 3 study. *J Clin Psychopharmacol*. 2016;36(2):130-140.
5. Data on File: RB-US-09-0010. Indivior Inc.
6. Andorn, Ann, Graham, Jay; Csernansky, John, et al. Monthly Extended-Release Risperidone (PERSERIS) in the Treatment of Schizophrenia, *J Clin Psychopharmacol*: Sept-Oct 2019, Vol, Issue 5 , p 428-43.

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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.

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.

Neuroleptic Malignant Syndrome, a potentially fatal symptom complex, has been reported with antipsychotic medications. Clinical manifestations include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (see full Prescribing Information). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Management should include immediate discontinuation of antipsychotic drugs and other drugs not

essential to concurrent therapy, intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems.

Tardive Dyskinesia (TD): 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. Less commonly, TD can develop after relatively brief treatment periods at low doses. 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.
- **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: Risperidone may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope. 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.

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

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

Seizures have been 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 pneumonia.

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

Disruption of Body Temperature Regulation has been attributed to antipsychotic agents. Use with caution in patients who will be exposed to temperature extremes.

ADVERSE REACTIONS

The most common adverse reactions in a clinical trial ($\geq 5\%$ 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 ($\geq 5\%$) were injection site pain and erythema.

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.

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.

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.

To report pregnancy or side effects associated with taking PERSERIS, please call 1-877-782-6966.

For more information about PERSERIS, please see accompanying Prescribing Information.

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