J-C Health Care Ltd.

Kibbutz Shefayim 6099000, ISRAEL
tel +972-9-959-1111
fax +972-9-958-3636

מרץ 2023

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון: Risperdal Consta 25mg, 37.5mg, 50mg
Solution for suspension for injection

בעל הרישום J-C Health Care Ltd. מבקש להודיעכם כי העלונים לרופא ולצרכן של התכשיר שבנדון עודכנו בפברואר 2023.

פרטי העדכון העיקריים מופיעים בהמשך *(טקסט שנוסף מסומן ב**אדום**, טקסט שהושמט מסומן כ~~טקסט כחול עם קו חוצה~~, טקסט שמיקומו בעלון שונה מסומן ב**ירוק**)* ,אך קיימים עדכונים נוספים.

ההתוויה המאושרת בישראל:

Risperdal consta is indicated for the treatment of schizophrenia and schizoaffective disorders.
Risperdal consta is indicated as monotherapy for the maintenance treatment of bipolar I disorder to delay occurrence of mood episodes.
Risperdal consta is indicated for adjunctive maintenance treatment to delay occurrence of mood episodes in patients with frequently relapsing bipolar disorder.

מרכיב פעיל:
RISPERIDONE

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug.

כמו כן, מצורפים לפרסום זה וניתן לקבל העתק מודפס שלהם באמצעות פנייה לבעל הרישום:
יאנסן ישראל בע"מ , קיבוץ שפיים, 6099000, טל': 09-9591111.

בברכה,
מירי חזן
רוקחת ממונה

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בהודעה זו כלולים העדכונים המהותיים בלבד. עיקרי העדכון נוגעים לעדכון עלון מדינת האסמכתא (US), להלן העדכונים:

<u>עלון לרופא</u>

3 DOSAGE FORMS AND STRENGTHS

RISPERDAL CONSTA® is available in dosage strengths of 25 mg, 37.5 mg, and 50 mg risperidone. It is provided as a single-use dose pack, consisting of a vial containing the risperidone microspheres, a pre-filled syringe containing 2 mL of diluent for RISPERDAL CONSTA®, a vial Adapter®, and two Terumo SurGuard® 3 Needles for intramuscular injection (a 21 G UTW 1-inch needle with needle protection device for deltoid administration and a 20 G TW 2-inch needle with needle protection device for gluteal administration).

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5.3 Neuroleptic Malignant Syndrome

Neuroleptic Malignant Syndrome (NMS), ~~A~~ a potentially fatal symptom complex, ~~sometimes referred to as Neuroleptic Malignant Syndrome (NMS)~~ has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status including delirium, ~~evidence of~~ and autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

~~The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases in which the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.~~

~~The management of NMS should include: (1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; (2) intensive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.~~

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If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. If NMS is suspected, immediately discontinue RISPERDAL CONSTA® and provide symptomatic treatment and monitoring.

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5.4 Tardive Dyskinesia

Tardive dyskinesia, ~~A~~ a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to ~~rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to~~ predict which patients will develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible ~~are believed to~~ increase ~~as~~ with the duration of treatment and the ~~total~~ cumulative dose. ~~of antipsychotic drugs administered to the patient increase. However, the~~ The syndrome can develop, ~~although much less commonly,~~ after relatively brief treatment periods, even at low doses. It may also occur after discontinuation of treatment.

Tardive dyskinesia ~~The syndrome~~ may remit, partially or completely, if antipsychotic treatment is discontinued ~~withdrawn~~. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome, ~~and thereby may~~ possibly masking the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, RISPERDAL CONSTA® should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients: (1) who suffer from a chronic illness that: ~~(1)~~ is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the ~~smallest~~ lowest dose and the shortest duration of treatment producing a satisfactory clinical response ~~should be sought~~. Periodically reassess ~~The~~ the need for continued treatment ~~should be reassessed periodically~~.

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If signs and symptoms of tardive dyskinesia appear in a patient treated with RISPERDAL CONSTA®, drug discontinuation should be considered. However, some patients may require treatment with RISPERDAL CONSTA® despite the presence of the syndrome.

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~~**5.14 Thrombotic Thrombocytopenic Purpura (TTP)**~~

~~A single case of TTP was reported in a 28 year-old female patient receiving oral RISPERDAL® in a large, open premarketing experience (approximately 1300 patients). She experienced jaundice, fever, and bruising, but eventually recovered after receiving plasmapheresis. The relationship to RISPERDAL® therapy is unknown.~~

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~~**5.17 Antiemetic Effect**~~

~~Risperidone has an antiemetic effect in animals; this effect may also occur in humans, and may mask signs and symptoms of overdosage with certain drugs or of conditions such as intestinal obstruction, Reye's syndrome, and brain tumor.~~

~~**5.18 Use in Patients with Concomitant Illness**~~

~~Clinical experience with RISPERDAL CONSTA® in patients with certain concomitant systemic illnesses is limited. Patients with Parkinson's Disease or Dementia with Lewy Bodies who receive antipsychotics, including RISPERDAL CONSTA®, are reported to have an increased sensitivity to antipsychotic medications. Manifestations of this increased sensitivity have been reported to include confusion, obtundation, postural instability with frequent falls, extrapyramidal symptoms, and clinical features consistent with the neuroleptic malignant syndrome.~~

~~Caution is advisable when using RISPERDAL CONSTA® in patients with diseases or conditions that could affect metabolism or hemodynamic responses. RISPERDAL CONSTA® has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from clinical studies during the product's premarket testing.~~

~~Increased plasma concentrations of risperidone and 9-hydroxyrisperidone occur in patients with severe renal impairment (creatinine clearance <30 mL/min/1.73 m^2) treated with oral RISPERDAL®; an increase in the free fraction of risperidone is also seen in patients with severe hepatic impairment. Patients with renal or hepatic impairment should be carefully titrated on oral RISPERDAL® before treatment with RISPERDAL CONSTA® is initiated at a dose of 25 mg. A lower initial dose of 12.5~~

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mg may be appropriate when clinical factors warrant dose adjustment, such as in patients with renal or hepatic impairment *[see Dosage and Administration (2.4)]*.

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6. ADVERSE REACTIONS

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- Thrombotic Thrombocytopenic Purpura (TTP) *[see Warnings and Precautions (5.14)]*
- Disruption of body temperature regulation *[see Warnings and Precautions (5.15)]*
- Avoidance of inadvertent injection into a blood vessel *[see Warnings and Precautions (5.16)*5.15*]*
- Antiemetic effect *[see Warnings and Precautions (5.17)]*
- Increased sensitivity in patients with Parkinson's disease or those with dementia with Lewy bodies *[see Warnings and Precautions (5.18)]*
- Diseases or conditions that could affect metabolism or hemodynamic responses *[see Warnings and Precautions (5.18)]*

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6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of risperidone; because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency: agranulocytosis, alopecia, anaphylactic reaction, angioedema, atrial fibrillation, blood cholesterol increased, blood triglycerides increased, catatonia, diabetes mellitus, diabetic ketoacidosis in patients with impaired glucose metabolism, drug withdrawal syndrome neonatal, dysgeusia, hypoglycemia, hypothermia, ileus, inappropriate antidiuretic hormone secretion, intestinal obstruction, jaundice, mania, pancreatitis, priapism, QT prolongation, sleep apnea syndrome, somnambulism, Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), thrombocytopenia, thrombotic thrombocytopenic purpura, urinary retention, and water intoxication. In addition, the following adverse reactions have been observed during postapproval use of RISPERDAL CONSTA®: cerebrovascular disorders, including cerebrovascular accidents, and diabetes mellitus aggravated.

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janssen
PHARMACEUTICAL COMPANIES
OF Johnson&Johnson

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Postmarketing cases of extrapyramidal symptoms (dystonia and dyskinesia) have been reported in patients concomitantly taking methylphenidate and risperidone when there was an increase or decrease in dosage, initiation, or discontinuation of either or both medications.

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7. DRUG INTERACTIONS

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7.6 Methylphenidate

Concomitant use with methylphenidate, when there is change in dosage of either medication, may increase the risk of extrapyramidal symptoms (EPS). Monitor for symptoms of EPS with concomitant use of RISPERDAL CONSTA® and methylphenidate *[see Adverse Reactions (6.2)]*.

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8. USE IN SPCESIFIC POPULATIONS

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8.6 Renal or Hepatic Impairment

In patients with renal or hepatic impairment, carefully titrate with oral risperidone prior to initiating treatment with RISPERDAL CONSTA® *[see Dosage and Administration (2.4)]*.

Patients with renal impairment may have less ability to eliminate risperidone than patients with normal renal function. Patients with impaired hepatic function may have an increase in the free fraction of risperidone, possibly resulting in an enhanced effect *[see Clinical Pharmacology (12.3)]*.

8.7 Patients with Parkinson's Disease or Lewy Body Dementia

Patients with Parkinson's Disease or Dementia with Lewy Bodies can experience increased sensitivity to RISPERDAL CONSTA®. Manifestations can include confusion, obtundation, postural instability with frequent falls, extrapyramidal symptoms, and clinical features consistent with neuroleptic malignant syndrome.

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<u>עלון לצרכן</u>

בנוסף לעדכונים בהתאם לעלון האסמכתא, התבצעה התאמה של נוסח ההתוויה להתוויה המאושרת.

1. למה מיועדת התרופה?

~~לטיפול בסכיזופרניה, בהפרעות סכיזואפקטיביות ובהפרעה דו קוטבית.~~
ריספרדל קונסטה מיועד לטיפול בסכיזופרניה ובהפרעות סכיזואפקטיביות.
ריספרדל קונסטה מיועד לטיפול יחיד אחזקתי להפרעה דו קוטבית, על מנת לעכב התרחשות של אפיזודות מצבי רוח.
ריספרדל קונסטה מיועד לטיפול תחזוקה משלים, על מנת לעכב את התרחשותן של אפיזודות מצבי רוח בחולים עם התקפים חוזרים תכופים של הפרעה דו קוטבית.

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2. לפי השימוש בתרופה

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אזהרות מיוחדות הנוגעות לשימוש בתרופה

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- מצב של בלבול, ירידה בהכרה, חום גבוה או נוקשות שרירים עלול להתרחש בעת שימוש בתרופה (מצב הנקרא Neuroleptic Malignant Syndrome). סימנים נוספים עשויים לכלול עלייה בקראטין פוספוקינאז, מיוגלובינוריה (רבדומיוליזיס) ואי ספיקת כליות חריפה. אם תופעה זו מתרחשת, יש לפנות מיד~~ית~~ לרופא וליידע אותו כי אתה נוטל ריספרדל קונסטה.
- ~~במהלך~~ שימוש ממושך, בריספרדל קונסטה עלול לגרום לעוויתות בלתי הפיכות לא רצוניות בפנים (Tardive dyskinesia). אם תופעה זו מתרחשת, יש לפנות לרופא. תופעה זו יכולה להתרחש גם לאחר הפסקת הטיפול.

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לפני הטיפול בריספרדל קונסטה ספר לרופא אם:

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- ~~סבלת אי פעם מתסמונת הכוללת את התסמינים הבאים: חום גבוה, קשיון שרירים, הזעה, או ירידה ברמת ההכרה (נקרא גם תסמונת נוירולפטית ממאירה [Neuroleptic Malignant Syndrome]).~~

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תגובות בין תרופתיות

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- מתילפנידאט, תרופות לטיפול בהפרעות קשב וריכוז (ADHD). דווחו תסמינים אקסטרה-פירמידליים (דיסטוניה ודיסקינזיה) במטופלים שנטלו מתילפנידאט וריספרדל קונסטה, כאשר היה שינוי במינון של אחת מהתרופות הללו.

~~**התרופות הבאות עלולות להגביר את השפעת הריספרידון:**~~

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4. תופעות לוואי

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- חמצת קטונית במטופלים עם הפרעה במטבוליזם של גלוקוז
- קטטוניה
- ארגמנת של קרישה וחסר טסיות (thrombotic thrombocytopenic purpura)
- תגובות חמורות באתר ההזרקה כולל אבצס, צלוליטיס, ציסטה, המטומה, נמק, גושים וכיב
- תגובה אנפילקטית
- דווחו תסמינים אקסטרה-פירמידליים (דיסטוניה ודיסקינזיה) במטופלים שנטלו מתילפנידאט וריספרדל קונסטה, כאשר היה שינוי במינון של אחת מהתרופות הללו.