IPT.04. Room 4.

Esketamine nasal spray▼: innovation in the management of treatment-resistant major depressive disorder

ECNP Industry Product Theatre Invitation

Monday 14th September, 15:00–15:30 CEST

Esketamine nasal spray is the first licensed antidepressant in 30 years that offers a new mode of action thought to target the glutamate system.[1–6]*

Join experienced experts as they discuss the use of esketamine nasal spray in the management of patients with treatment-resistant major depressive disorder, and share experience from their clinics.

An international faculty will share clinical data and explore the practicalities of using esketamine nasal spray, from choosing the right patients and managing expectations, to setting up the clinic and managing potential side effects.

Professor
Allan Young
King's College London,
UK

Professor
Siegfried Kasper
Medical University of Vienna
Austria

Associate Professor
Anders Luts
University of Lund,
Sweden

To find out more information about the Industry Product Theatre, and to join, please access the ECNP congress programme **here** or contact your local Janssen representative.

Industry Product Theatre on the occasion of the 33rd ECNP Congress *Virtual*, with educational financial support provided by Janssen.

*Following the development and approval of the SSRI fluoxetine in 1987, approved treatments (including 'atypical' antidepressants such as mirtazapine, agomelatine, etc.) have continued to primarily target the monoaminergic system.[2–6] In contrast, esketamine nasal spray acts as an antagonist of the NMDA glutamate receptor and is proposed to lead to an increase in AMPAR stimulation and neurotrophic signalling.[1]
AMPAR: apha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; NMDA: N-Methyl-d-aspartic acid; SSRI: selective serotonin reuptake inhibitor.

1. Esketamine nasal spray Summary of Product Characteristics. December 2019; **2.** Hillhouse TM, Porter JH. *Exp Clin Psychopharmacol*. 2015;23:1–21; **3.** Agomelatine Summary of Product Characteristics. 2019; **4.** Mirtazapine 15 mg Summary of Product Characteristics. 2018; **5.** Harmer CJ, et al. *Lancet Psychiatry*. 2017;4:409–18; **6.** Whiting DW, Cowen DJ. *Psychiatrist*. 2013;37:356–8.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Prescribing information is available on the reverse and adverse events should be reported to Janssen and the local regulatory authorities.

Janssen Neuroscience
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

SPRAVATO ▼ ABBREVIATED PRESCRIBING INFORMATION BASED ON THE EU SUMMARY OF PRODUCT CHARACTERISTICS

SPRAVATO 28 mg NASAL SPRAY, SOLUTION

ACTIVE INGREDIENT(S): 28 mg esketamine

Please refer to Summary of Product Characteristics (SmPC) before prescribing.

INDICATION(S):
SPRAVATO, in combination with a SSRI or SNRI, is indicated for adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode.

DOSAGE & ADMINISTRATION: The decision to prescribe Spravato should be determined by a psychiatrist. Spravato is intended to be self-administered by the patient under the direct supervision of a healthcare professional. A treatment session consists of nasal administration of Spravato and a post-administration observation period. Both administration and post-administration observation of Spravato should be carried out in an appropriate clinical setting. Prior to dosing with Spravato blood pressure should be assessed. If baseline blood pressure is elevated the risks of short-term increases in blood pressure and benefit of Spravato treatment should be considered. Patients with clinically significant or unstable cardiovascular or respiratory conditions require additional precautions (see section SPECIAL WARNINGS & PRECAUTIONS). After dosing with Spravato, blood pressure should be reassessed at approximately 40 minutes and subsequently as clinically warranted. Because of the possibility of sedation, dissociation and elevated blood pressure, patients must be monitored by a healthcare professional until the patient is considered clinically stable and ready to leave the healthcare setting. Dose adjustments should be made based on efficacy and tolerability to the previous dose. During the maintenance phase, Spravato dosing should be individualised to the lowest frequency to maintain remission/response.
Recommended dosing for Spravato in adults <65 years: Induction phase*: *Weeks 1-4*: Starting day 1 dose: 56 mg and Subsequent doses: 56 mg or 84 mg twice a week. Maintenance phase**: *Weeks 5-8*: 56 mg or 84 mg once weekly. *From week 9*: 56 mg or 84 mg every 2 weeks or once weekly. **Recommended dosing for Spravato in adults ≥65 years:** Induction phase*: *Weeks 1-4*: Starting day 1 dose: 28 mg and Subsequent doses: 28 mg, 56 mg or 84 mg twice a week, all dose changes should be in 28 mg increments. Maintenance phase**: *Weeks 5-8*: 28 mg, 56 mg or 84 mg once weekly, all dose changes should be in 28 mg increments. *From week 9*: 28 mg, 56 mg or 84 mg every 2 weeks or once weekly, all dose changes should be in 28 mg increments. Note: * Evidence of therapeutic benefit should be evaluated at the end of induction phase to determine need for continued treatment. ** The need for continued treatment should be reexamined periodically.

After depressive symptoms improve, treatment is recommended for at least 6 months.

Food and liquid intake recommendations prior to administration: Since some patients may experience nausea and vomiting after administration of Spravato, patients should be advised not to eat for at least 2 hours before administration and not to drink liquids at least 30 minutes prior to administration. ***Nasal corticosteroid or nasal decongestant:*** Patients who require a nasal corticosteroid or nasal decongestant on a dosing day should be advised not to administer these medicinal products within 1 hour before Spravato administration. ***Missed treatment session(s):*** In case one or two treatment sessions are missed, the next session should be scheduled when the next session was scheduled to occur based on current treatment frequency. If more than 2 treatment sessions have been missed, per clinical judgment, adjustment of the dose or frequency of Spravato may be clinically appropriate.

Special populations: ***Hepatic impairment:*** No dose adjustment is necessary in patients with mild (Child Pugh class A) or moderate (Child Pugh class B) hepatic impairment. However, the maximum dose of 84 mg should be used with caution in patients with moderate hepatic impairment. Spravato has not been studied in patients with severe hepatic impairment (Child-Pugh class C). Use in this population is not recommended. ***Renal impairment:*** No dose adjustment is necessary in patients with mild to severe renal impairment. Patients on dialysis were not studied. ***Paediatric population:*** The safety and efficacy of Spravato in paediatric patients aged 17 years and younger have not been established. There is no relevant use of Spravato in children less than 7 years of age in treatment-resistant depression. ***Race:*** **Recommended Dosing for Spravato in Adults of Japanese Ancestry:** Induction phase: *Weeks 1-4*: Starting day 1 dose: 28 mg and Subsequent doses: 28 mg, 56 mg or 84 mg twice a week, all dose changes should be in 28 mg increments. Evidence of therapeutic benefit should be evaluated at the end of induction phase to determine need for continued treatment. Maintenance phase: *Weeks 5-8*: 28 mg, 56 mg or 84 mg once weekly, all dose changes should be in 28 mg increments. *From week 9*: 28 mg, 56 mg or 84 mg every 2 weeks or once weekly, all dose changes should be in 28 mg increments. The need for continued treatment should be reexamined periodically.

Method of administration: Spravato is for nasal use only. The nasal spray device is a single-use device that delivers a total of 28 mg of esketamine, in two sprays (one spray per nostril). To prevent loss of medicinal product, the device should not be primed before use. It is intended for administration by the patient under the supervision of a healthcare professional, using 1 device (for a 28 mg dose), 2 devices (for a 56 mg dose) or 3 devices (for an 84 mg dose), with a 5-minute rest between use of each device. If sneezing occurs immediately after administration, a replacement device should not be used. If administration in the same nostril occurs, a replacement device should not be used.

CONTRAINDICATIONS: Hypersensitivity to the active substance, ketamine, or to any of the excipients of SPRAVATO. Patients for whom an increase in blood pressure or intracranial pressure poses a serious risk: Patients with aneurysmal vascular disease (including intracranial, thoracic, or abdominal aorta, or peripheral arterial vessels); Patients with history of intracerebral haemorrhage; Recent (within 6 weeks) cardiovascular event, including myocardial infarction (MI).
SPECIAL WARNINGS & PRECAUTIONS: ***Neuropsychiatric and motor impairments***: Spravato has been reported to cause somnolence, sedation, dissociative symptoms, perception disturbances, dizziness, vertigo and anxiety during the clinical trials. These effects may impair attention, judgment, thinking, reaction speed and motor skills. At each treatment session, patients should be monitored under the supervision of a healthcare professional to assess when the patient is considered stable based on clinical judgement. ***Respiratory depression***: Respiratory depression may occur at high doses following rapid intravenous injection of esketamine or ketamine when used for anaesthesia. Rare cases of deep sedation have been reported with Spravato. Concomitant use of Spravato with CNS depressants may increase the risk for sedation. Close monitoring is required for sedation and respiratory depression. ***Effect on blood pressure***: Spravato can cause transient increases in systolic and/or diastolic blood pressure which peak at approximately 40 minutes after administration and last approximately 1-2 hours. A substantial increase in blood pressure could occur after any treatment session. Before prescribing Spravato, patients with cardiovascular and cerebrovascular conditions should be carefully assessed to determine whether the potential benefits of Spravato outweigh its risks. After administration, if blood pressure remains elevated, assistance should promptly be sought from practitioners experienced in blood pressure management. Patients who experience symptoms of a hypertensive crisis should be referred immediately for emergency care. ***Patients with clinically significant or unstable cardiovascular or respiratory conditions***: Only initiate treatment with Spravato in patients with clinically significant or unstable cardiovascular or respiratory conditions if the benefit outweighs the risk. In these patients, Spravato should be administered in a setting where appropriate resuscitation equipment and healthcare professionals with training in cardiopulmonary resuscitation are available. ***Suicide/suicidal thoughts or clinical worsening***: Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs, therefore, patients should be closely monitored. It is general clinical experience that the risk of suicide may increase in the early stages of recovery. Patients with a history of suicide-related events or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts and should receive careful monitoring during treatment. Close supervision of patients and in particular those at high risk should accompany treatment especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted to the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present. ***Drug abuse, dependence, withdrawal***: Spravato contains esketamine and may be subject to abuse and diversion. Individuals with a history of drug abuse or dependence may be at greater risk for abuse and misuse of Spravato. Prior to prescribing Spravato, each patient's risk for abuse or misuse should be assessed and patients receiving esketamine should be monitored for the development of behaviours or conditions of abuse or misuse, including drug seeking behaviour, while on therapy. Ketamine has been reported to be abused. Dependence and tolerance have been reported with prolonged use of ketamine. ***Other populations at risk***: Spravato should be used with caution in patients with the following conditions. These patients should be carefully assessed before prescribing Spravato and treatment initiated only if the benefit outweighs the risk: Presence or history of psychosis; Presence or history of mania or bipolar disorder; Hyperthyroidism that has not been sufficiently treated; History of brain injury, hypertensive encephalopathy, intrathecal therapy with ventricular shunts, or any other condition associated with increased intracranial pressure. ***Elderly (65 years of age and older)***: Elderly patients treated with Spravato may have a greater risk of falling once mobilised, therefore, these patients should be carefully monitored. ***Severe hepatic impairment:*** Due to expected increase in exposure and lack of clinical experience, Spravato is not recommended in patients with Child-Pugh class C (severe) hepatic impairment. Hepatotoxicity has been reported with chronic ketamine use, therefore, the potential for such an effect due to long-term use of Spravato cannot be excluded. ***Urinary tract symptoms***: Urinary tract and bladder symptoms have been reported with Spravato use. It is recommended to monitor for urinary tract and bladder symptoms during the course of treatment and refer to an appropriate healthcare provider when symptoms persist.
SIDE EFFECTS: ***Very Common***: dissociation, dizziness, headache, dysgeusia, somnolence, hypoaesthesia, vertigo, nausea, vomiting ***Common:*** euphoric mood, agitation, anxiety, illusion, irritability, panic attack, time perception altered, hallucination including visual hallucination, derealization, mental impairment, tremor, lethargy, dysarthria, paraesthesia, sedation, vision blurred, hyperacusis, tinnitus, tachycardia, hypertension, nasal discomfort, nasal dryness including nasal crusting, nasal pruritus, dry mouth, hypoaesthesia oral, hyperhidrosis, pollakiuria, dysuria, micturition urgency, feeling abnormal, feeling drunk, feeling of body temperature change, blood pressure increased.

Refer to the SmPC for other side effects.

PREGNANCY: Spravato is not recommended during pregnancy and in women of childbearing potential not using contraception. There are no or limited data on the use of esketamine in pregnant women. Animal studies have shown that ketamine, the racemic mixture of arketamine and esketamine, induces neurotoxicity in developing foetuses. A similar risk with esketamine cannot be excluded. If a woman becomes pregnant while being treated with Spravato, treatment should be discontinued, and the patient should be counselled about the potential risk to the foetus and clinical/therapeutic options as soon as possible.

LACTATION: It is unknown whether esketamine is excreted in human milk. Data in animals have shown excretion of esketamine in milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Spravato therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

FERTILITY: Animal studies showed that fertility and reproductive capacities were not adversely affected by esketamine.

Effects on ability to drive and use machines: Spravato has a major influence on the ability to drive and use machines. Before Spravato administration, patients should be instructed not to engage in potentially hazardous activities requiring complete mental alertness and motor coordination, such as driving a vehicle or operating machinery, until the next day following a restful sleep.

INTERACTIONS: Concomitant use of Spravato with CNS depressants (e.g., benzodiazepines, opioids, alcohol) may increase sedation, which therefore should be closely monitored. Blood pressure should be closely monitored when Spravato is used concomitantly with psychostimulants (e.g., amphetamines, methylphenidate, modafanil, armodafinil) or other medicinal products that may increase blood pressure (e.g. xanthine derivatives, ergometrine, thyroid hormones, vasopressin, or MAOIs, such as, tranylcypromine, selegiline, phenelzine).

LEGAL CLASSIFICATION: country specific.

MARKETING AUTHORISATION NUMBER(S): EU/1/19/1410/001-004

MARKETING AUTHORISATION HOLDER: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium.

PACKS & PRICE: *country specific.*

Spravato 28 mg Nasal Spray Solution: Pack sizes of 1, 2, 3, or 6 nasal spray devices. Products mentioned in this document may not be registered in all countries. Prescribing Information may vary per country. Health Care Providers must refer to their country prescribing information.

Prescribing information generation date: February 2020

Based on December 2019 EU Summary of Product Characteristics