CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

211243Orig1s006

Trade Name:	SPRAVATO
Generic or Proper Name:	(esketamine hydrochloride)
Sponsor:	Janssen Pharmaceuticals Inc.
Approval Date:	January 03, 2022
Indication:	SPRAVATO® is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated, in conjunction with an oral antidepressant, for the treatment of: • Treatment-resistant depression (TRD) in adults. • Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior. Limitations of Use: • The effectiveness of SPRAVATO in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of SPRAVATO does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of SPRAVATO. • SPRAVATO is not approved as an anesthetic agent. The safety and effectiveness of SPRAVATO as an anesthetic agent have not been established.

CENTER FOR DRUG EVALUATION AND RESEARCH

211243Orig1s006

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211243Orig1s006

APPROVAL LETTER

NDA 211243/S-006

SUPPLEMENT APPROVAL

Janssen Pharmaceuticals, Inc.
Jadwiga Martynowicz, DM, MS
Senior Director, Global Regulatory Affairs-Neuroscience
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Dear Ms. Martynowicz:

Please refer to your supplemental new drug application (sNDA) dated and received October 11, 2021, and your amendments, submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Spravato (esketamine) nasal spray 28 mg single-use device.

This "Changes Being Effected" supplemental new drug application provides for proposed modifications to the approved Spravato (esketamine) risk evaluation and mitigation strategy (REMS). We acknowledge that your application included a rationale to support the proposed REMS modifications.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Spravato was originally approved on March 5, 2019. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of changes to the Spravato REMS Patient Monitoring Form, including revising the format of some of the data-capturing fields and adding a field to capture the lot number field of Spravato.

Your proposed modified REMS, submitted on October 11, 2021, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on March 5, 2019.

There are no changes to the REMS assessment plan described in our July 31, 2020, letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous

REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 211243 REMS ASSESSMENT METHODOLOGY

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 211243 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR NDA 211243/ S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or
NEW SUPPLEMENT FOR NDA 211243/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 211243/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)

FOR NDA 211243/S-000
REMS ASSESSMENT PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA 211243

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

FDA can accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST).

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Ermias Zerislassie, Regulatory Project Manager, at 301-796-2770.

Sincerely,

{See appended electronic signature page}

Tiffany R. Farchione, MD
Director
Division of Psychiatry
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE(S):

- REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

BERNARD A FISCHER on behalf of TIFFANY R FARCHIONE
01/03/2022 10:02:45 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211243Orig1s006

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

SPRAVATO (esketamine) REMS Program

I. Administrative Information

Application Number: NDA 211,243
Application Holder: Janssen Pharmaceuticals, Inc.
Initial REMS Approval: 3/2019
Most recent REMS Update: 1/2022

II. REMS Goal

The goal of the REMS is to mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by SPRAVATO administration, and abuse and misuse of SPRAVATO by:

- Ensuring that SPRAVATO is only dispensed and administered to patients in a medically supervised healthcare setting that monitors these patients.
- Ensuring pharmacies and healthcare settings that dispense SPRAVATO are certified.
- Ensuring patients are informed about the serious adverse outcomes resulting from sedation and dissociation and need for monitoring.
- Enrolling all patients who receive treatment in an outpatient healthcare setting in a registry to further characterize the risks and support safe use.

III. REMS Requirements

Janssen Pharmaceuticals, Inc. must ensure that healthcare settings, patients, pharmacies, and wholesalers-distributors comply with the following requirements:

---

1. Healthcare settings that dispense SPRAVATO for outpatient use must:

To become certified to dispense	1. Have a prescriber onsite during SPRAVATO administration and monitoring. 2. Have healthcare provider(s) onsite to monitor patients. 3. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the healthcare setting. 4. Have the authorized representative review the SPRAVATO prescribing information and REMS Program Overview. 5. Have the authorized representative enroll in the REMS Program by completing the Outpatient Healthcare Setting Enrollment Form and submitting it to the REMS Program. 6. Establish processes and procedures to enroll the patient in the REMS Program. 7. Establish processes and procedures to counsel the patient on the need for enrollment, monitoring, and risks of sedation and dissociation, and changes in vital signs.

	8. Establish processes and procedures to verify the patient is enrolled in the REMS Program before each administration and that SPRAVATO is not dispensed for use outside the certified healthcare setting. 9. Establish processes and procedures to complete and submit the Patient Monitoring Form after each administration within 7 calendar days. 10. Train all relevant staff involved in prescribing, dispensing and administering SPRAVATO on 1) Counseling the patient on the need for monitoring and risks of sedation and dissociation, and changes in vital signs; 2) Patient administration under the supervision of a healthcare provider; and 3) Monitoring for resolution of sedation and dissociation and changes in vital signs for a minimum of 2 hours. 11. Establish processes and procedures to identify all staff involved in prescribing, dispensing, and administering SPRAVATO and ensure they are trained on 1) Counseling the patient on the need for monitoring and risks of sedation and dissociation, and changes in vital signs; 2) Patient administration under the supervision of a healthcare provider; 3) Monitoring for resolution of sedation and dissociation and changes in vital signs for a minimum of 2 hours.
Before treatment initiation (first dose)	12. Counsel the patient on the risks and need for monitoring for resolution of sedation and dissociation and changes in vital signs. 13. Enroll the patient by completing and submitting the Patient Enrollment Form to the REMS Program.
Before administering	14. Counsel the patient on the need for monitoring for resolution of sedation and dissociation, and changes in vital signs. 15. Verify the patient is enrolled in the REMS Program through the processes and procedures established as a requirement of the REMS Program.
During and after administering, for at least 2 hours	16. Assess the patient for administration of SPRAVATO and resolution of sedation and dissociation, and changes in vital signs.
After administering, within 7 calendar days	17. Document and submit to the REMS Program using the Patient Monitoring Form.
To maintain certification to dispense	18. Have any new authorized representative enroll in the REMS Program by completing the Outpatient Healthcare Setting Enrollment Form.
At all times	19. Not dispense SPRAVATO for use outside the certified healthcare setting. 20. Not distribute, transfer, loan, or sell SPRAVATO. 21. Maintain records documenting staff's completion of training.

	22. Maintain records that all processes and procedures are in place and are being followed. 23. Maintain records of all shipments of SPRAVATO received and dispensing information including patient name, dose, number of devices, and date administered. 24. Comply with audits carried out by Janssen Pharmaceuticals, Inc. or a third party acting on behalf of Janssen Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

2. Healthcare settings that dispense SPRAVATO for inpatient use (including emergency departments within certified healthcare settings) must:

To become certified to dispense	1. Have a prescriber onsite during SPRAVATO administration and monitoring. 2. Have healthcare provider(s) onsite to monitor patients. 3. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the healthcare setting. 4. Have the authorized representative review the SPRAVATO prescribing information and REMS Program Overview. 5. Have the authorized representative enroll in the REMS Program by completing and submitting the Inpatient Healthcare Setting Enrollment Form. 6. Establish processes and procedures to counsel the patient on the need for monitoring and risks of sedation and dissociation, and changes in vital signs. 7. Establish processes and procedures to verify SPRAVATO is not dispensed for use outside the certified healthcare setting. 8. Train all relevant staff involved in prescribing, dispensing and administering SPRAVATO on 1) Counseling the patient on the need for monitoring,risks of sedation and dissociation, changes in vital signs, and the need to have arrangements to safely leave the healthcare setting and not engage in potentially hazardous activities; 2) Patient administration under the supervision of a healthcare provider; and 3) Monitoring for resolution of sedation and dissociation and changes in vital signs for a minimum of 2 hours.
Before administering	9. Counsel the patient on the need for monitoring for resolution of sedation and dissociation, and changes in vital signs and the need to have arrangements to safely leave the healthcare setting and not engage in potentially hazardous activities
During and after administering, for at least 2 hours	10. Assess the patient for administration of SPRAVATO and resolution of sedation and dissociation, and changes in vital signs.

To maintain certification to dispense	11. Have any new authorized representative enroll in the REMS Program by completing the Inpatient Healthcare Setting Enrollment Form.
At all times	12. Not dispense SPRAVATO for use outside the certified healthcare setting. 13. Not distribute, transfer, loan, or sell SPRAVATO. 14. Maintain records documenting staff's completion of training. 15. Maintain records that all processes and procedures are in place and are being followed. 16. Maintain records of all shipments of SPRAVATO received and dispensing information including patient name, dose, number of devices, and date administered. 17. Comply with audits carried out by Janssen Pharmaceuticals, Inc. or a third party acting on behalf of Janssen Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

3. Patients who are prescribed SPRAVATO:

Before treatment initiation (first dose)	1. Receive counseling from a healthcare provider on risks and the need for monitoring for resolution of sedation and dissociation, and changes in vital signs. 2. For outpatients: Enroll in the REMS Program by completing the Patient Enrollment Form with a healthcare provider. Enrollment information will be provided to the REMS Program.
During treatment, before each dose	3. Receive counseling from a healthcare provider on the need for monitoring for resolution of sedation and dissociation; and change in vital signs.
During treatment, during and after administration for at least 2 hours	4. Be monitored for taking SPRAVATO, resolution of sedation and dissociation, and changes in vital signs at the healthcare setting.

4. Pharmacies that dispense SPRAVATO must:

To become certified to dispense	1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the pharmacy. 2. Have the authorized representative enroll in the REMS Program by completing the Pharmacy Enrollment Form and submitting it to the REMS Program. 3. Establish processes and procedures to verify that a healthcare setting is certified in the REMS Program before dispensing SPRAVATO. 4. Train all relevant staff involved in dispensing that SPRAVATO must only be dispensed to a certified healthcare setting.
Before dispensing	5. Verify that the healthcare setting is certified through the processes and procedures established as a requirement of the REMS Program.

At all times	6. Not distribute, transfer, loan or sell SPRAVATO except to certified dispensers. 7. Not dispense SPRAVATO for use outside a certified healthcare setting. 8. Maintain records documenting staff's completion of training. 9. Maintain records that all processes and procedures are in place and are being followed. 10. Maintain records of all shipments of SPRAVATO received and dispensing information including patient name, dose, number of devices, and date dispensed. 11. Comply with audits carried out by Janssen Pharmaceuticals, Inc. or third party acting on behalf of Janssen Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

5. Wholesalers-distributors that distribute SPRAVATO must:

To be able to distribute	1. Establish processes and procedures to ensure that SPRAVATO is distributed only to certified healthcare settings and certified pharmacies. 2. Train all relevant staff involved in distributing on the REMS Program requirements.
At all times	3. Distribute only to certified healthcare settings and certified pharmacies. 4. Maintain and submit records of all shipments of SPRAVATO. 5. Comply with audits carried out by Janssen Pharmaceuticals, Inc. or a third party acting on behalf of Janssen Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

Janssen Pharmaceuticals, Inc. must provide training to health care settings that dispense SPRAVATO.

The training includes the following educational material: REMS Program Overview. The training must be provided online and in hardcopy format by mail or fax.

To support REMS Program operations, Janssen Pharmaceuticals, Inc. must:

1. Establish and maintain a REMS Program website, www.SPRAVATOREMS.com. The REMS Program website must include the capability to complete healthcare setting and pharmacy certification online, patient enrollment online, the capability to provide patient monitoring information online, and to print the Prescribing Information, Medication Guide and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS program website. The REMS program website must not link back to the promotional product website(s).

2. Make the REMS program website fully operational and all REMS materials available through the website and coordinating center.

3. Establish and maintain a REMS coordinating center for REMS participants at 1–855-382-6022.

4. Establish and maintain a validated and secure database of all REMS participants who are enrolled and/or certified in the REMS Program.

5. Ensure healthcare settings and pharmacies are able to enroll and certify in the REMS Program online or by fax.

6. Ensure healthcare providers in outpatient healthcare settings are able to enroll patients by fax and online.

7. Ensure outpatient healthcare settings are able to submit the Patient Monitoring Form by fax and online.

8. Notify healthcare settings and pharmacies within 7 calendar days after they become certified in the REMS.

9. Provide the Outpatient Healthcare Setting Enrollment Form, Inpatient Healthcare Setting Enrollment Form, Pharmacy Enrollment Form, REMS Program Overview and Prescribing Information to REMS participants who (1) attempt to dispense SPRAVATO and are not yet certified, or (2) inquire about how to become certified.

10. Provide public access to a database of certified healthcare settings and pharmacies.

11. Provide certified pharmacies access to the database of certified healthcare settings.

12. Provide certified healthcare settings access to the database of certified pharmacies and enrolled patients.

13. Provide authorized wholesalers-distributors access to a database of certified pharmacies and healthcare settings.

14. Establish and maintain a registry, which includes a reporting and collection system for all patients treated in outpatient healthcare settings, to provide information on the incidence of adverse outcomes from sedation and dissociation.

15. Ensure that once a report suggestive of adverse outcomes from sedation or dissociation is received, Janssen Pharmaceuticals, Inc. follows up with the healthcare provider to obtain all required data for the registry.

To ensure REMS participants' compliance with the REMS program, Janssen Pharmaceuticals, Inc. must:

16. Notify outpatient healthcare settings if Patient Monitoring Forms have not been received by the REMS Program in the last 60 calendar days from the date of submission of the Patient Enrollment Form.
17. Ensure every 60 calendar days from the date of submission of the Patient Enrollment Form that all expected monitoring forms are received for each patient.

18. Verify annually that the authorized representative's name and information correspond to the authorized healthcare setting or pharmacy. If the authorized representative changes at any time, the healthcare setting or pharmacy must be required to re-certify with a new authorized representative.
19. Maintain adequate records to demonstrate that REMS requirements have been met, including but not limited to records of: drug distribution and dispensing; certification of healthcare settings and pharmacies; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.
20. Establish a plan for addressing non-compliance with the REMS Program requirements.

21. Monitor pharmacies, healthcare settings, and wholesalers/distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.
22. Audit 15% or 50 healthcare settings (whichever is greater), 15% or 50 pharmacies (whichever is greater), and data from all wholesalers-distributors that have ordered/dispensed SPRAVATO at 12 months from date of first commercial distribution and annually thereafter to ensure that all REMS processes are in place, functioning and support the REMS requirements. To be audited, healthcare setting must have received at least one shipment of SPRAVATO in the past 12 months and not have been previously audited in the past 3 years.
23. Take reasonable steps to improve implementation of and compliance with the requirements in the SPRAVATO REMS Program based on monitoring and evaluation of the SPRAVATO REMS Program.

IV. REMS Assessment Timetable

Janssen Pharmaceuticals, Inc. must submit REMS assessments at 6 months and 12 months from the date of initial approval of the REMS and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Janssen Pharmaceuticals, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the SPRAVATO REMS:

Enrollment Forms

Healthcare Setting:

1. Outpatient Healthcare Setting Enrollment Form
2. Inpatient Healthcare Setting Enrollment Form

Patient:

3. Patient Enrollment Form

Pharmacy:

4. Pharmacy Enrollment Form

Training and Educational Materials

Healthcare Setting:

5. REMS Program Overview

Pharmacy:

6. REMS Program Overview

Patient Care Forms

7. Patient Monitoring Form

Other Materials

8. REMS Program Website

SPRAVATO® REMS

Outpatient Healthcare Setting Enrollment Form

INSTRUCTIONS:

1. Review the *SPRAVATO® Prescribing Information* and the *SPRAVATO® REMS Program Overview*
2. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091

This form is intended only for Outpatient Medical Offices and Clinics.
Emergency departments within hospitals are certified through the Inpatient Healthcare Setting enrollment.

Indicates Required Field

Healthcare Setting Information

Healthcare Setting Name*:		
Healthcare Setting Address 1*:	Address Line 2:	
City*:	State*:	ZIP*:
Healthcare Setting Telephone Number*:	Healthcare Setting Website URL:	
DEA License Number* (associated with the Healthcare Setting address):	Name of DEA License Holder (if different from Healthcare Setting Name):	DEA License Expiration Date (MM/DD/YYYY)*:

Healthcare Setting Type*: (select all that apply)
☐ Mental Health Facility ☐ Outpatient Clinic ☐ Independent Practice ☐ Group Practice
☐ Other:_____

If your healthcare setting is **an independent (private) practice, or group practice, or outpatient clinic**, how does your practice intend to acquire SPRAVATO® for patients? (Select all that apply)

☐ By sending a patient-specific prescription for SPRAVATO® CIII (controlled substance) to a REMS-certified pharmacy, have that pharmacy deliver patient-name product to your practice, and follow all required State and Federal DEA laws and regulations.

☐ By acquiring SPRAVATO® CIII (controlled substance) as bulk supply directly from a SPRAVATO® REMS-qualified distributor, and follow all required State and Federal DEA laws and regulations.

For each additional healthcare setting where SPRAVATO® will be delivered, dispensed, and administered within your healthcare system for which the same Authorized Representative will be responsible, you will **need to** complete page 3.

Your healthcare setting information will be shared with Janssen's patient support and distribution partners, to allow your healthcare setting to purchase product.

Your healthcare setting information (name, location, and phone number) will be listed on a location finder, as a certified healthcare setting, available to healthcare professionals and patients seeking treatment with SPRAVATO®. **If you do not want your information listed, please call SPRAVATO® REMS at 1-855-382-6022.**

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Reference ID: 4913334

SPRAVATO® REMS

Outpatient Healthcare Setting Enrollment Form

** Indicates Required Field*

Healthcare Setting Authorized Representative Information

First Name*:	MI:	Last Name*:

Credentials*: ☐ Physician ☐ Physician Assistant ☐ Nurse ☐ Pharmacist ☐ Other: _____

Telephone Number*:	EXT:	Fax*:	Email Address*:

Healthcare Setting Alternate Contact

First Name:	Last Name:

Telephone Number:	EXT:	Fax:	Email Address:

Healthcare Setting Authorized Representative Agreement

I am the Authorized Representative designated by my Healthcare Setting to oversee implementation and coordinate the activities of the SPRAVATO® REMS. By signing this form, I agree, on behalf of myself and my Healthcare Setting, to comply with all REMS Requirements:

I will:

- Review the SPRAVATO® Prescribing Information and REMS Program Overview.
- Enroll in the SPRAVATO® REMS by completing this form *and* submitting this form to the SPRAVATO® REMS.
- Have a prescriber onsite during SPRAVATO® administration and monitoring.
- Have a healthcare provider(s) onsite to monitor each patient for at least 2 hours following administration of SPRAVATO® for resolution of sedation and dissociation, and changes in vital signs.
- **Establish processes and procedures** and **train** all relevant staff involved in prescribing, dispensing, and administering SPRAVATO® to ensure that the following takes place in my Healthcare Setting:
  - Prior to the patient receiving SPRAVATO®, a healthcare provider counsels the patient on the need for enrollment, monitoring, risks of sedation and dissociation, and changes in vital signs.
  - All patients are enrolled in the SPRAVATO® REMS by completing and submitting the *Patient Enrollment Form* with their prescriber.
  - Verify the patient is enrolled in the REMS before dispensing SPRAVATO® for patient administration.
  - The patient administers SPRAVATO® under the direct supervision of a healthcare provider.
  - A healthcare provider monitors every patient for at least 2 hours for resolution of sedation and dissociation and changes in vital signs after every dose.
  - A *Patient Monitoring Form* is submitted to the SPRAVATO® REMS for every patient within 7 days following administration of every dose.
  - Notify the SPRAVATO® REMS in advance if patient treatment will be transferred from one REMS-certified Healthcare Setting to another REMS-certified Healthcare Setting.
  - SPRAVATO® is not dispensed for use outside the Healthcare Setting.
  - If the authorized representative changes, have the new authorized representative re-certify the Outpatient Healthcare Setting into the REMS by completing the *Outpatient Healthcare Setting Enrollment Form*.
  - Not distribute, transfer, loan, or sell SPRAVATO®.
- Maintain records documenting staff's completion of training.
- Maintain records that all processes and procedures are in place and are being followed.
- Maintain records of all shipments of SPRAVATO® received and dispensing information including the patient name, dose, number of devices, and date administered.
- Comply with audits carried out by Janssen Pharmaceuticals, Inc., or a third party acting on behalf of Janssen Pharmaceuticals, Inc., to ensure that all processes and procedures are in place and are being followed.

Name (please print):

Authorized Representative Signature*:	**Date*:**

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SPRAVATO® REMS

Outpatient Healthcare Setting Enrollment Form

Use this form to add each additional healthcare setting location for which the same Authorized Representative will be responsible.

** Indicates Required Field*

Additional Healthcare Setting

Authorized Representative First Name*:	MI:	Last Name*:
Authorized Representative Email:		
Healthcare Setting Name *:		
Healthcare Setting Address 1*:		Address Line 2:
City*:	State*:	ZIP*:
Healthcare Setting Telephone Number*:		Healthcare Setting Website URL:
DEA License Number* (associated with the Healthcare Setting address):	Name of DEA License Holder (if different from Healthcare Setting Name):	DEA License Expiration Date (MM/DD/YYYY)*:

Healthcare Setting Type*: (select all that apply)
☐ Mental Health Facility ☐ Outpatient Clinic ☐ Independent Practice ☐ Group Practice
☐ Other:_____

If your healthcare setting is **an independent (private) practice, or group practice, or outpatient clinic**, how does your practice intend to acquire SPRAVATO® for patients? (Select all that apply)

☐ By sending a patient-specific prescription for SPRAVATO® CIII (controlled substance) to a REMS-certified pharmacy, have that pharmacy deliver patient-name product to your practice, and follow all required State and Federal DEA laws and regulations.

☐ By acquiring SPRAVATO® CIII (controlled substance) as bulk supply directly from a SPRAVATO® REMS-qualified distributor, and follow all required State and Federal DEA laws and regulations.

Additional Alternate Contact Information

First Name:		Last Name:	
Telephone Number:	EXT:	Fax:	Email Address:

Your healthcare setting information will be shared with Janssen's patient support and distribution partners, to allow your outpatient healthcare setting to purchase product.

Your healthcare setting information (name, location, and phone number) will be listed on a location finder, as a certified outpatient healthcare setting, available to healthcare professionals and patients seeking treatment with SPRAVATO®. **If you do not want your information listed, please call SPRAVATO® REMS at 1-855-382-6022.**

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Reference ID: 4913334

SPRAVATO® REMS

Inpatient Healthcare Setting Enrollment Form

INSTRUCTIONS:

1. Review the *SPRAVATO® Prescribing Information* and the *SPRAVATO® REMS Program Overview*
2. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091

As an Inpatient Healthcare Setting (with inpatient units, emergency department, etc.), your Inpatient Pharmacy, operating under the same Drug Enforcement Administration (DEA) license and physical location, will be considered certified once this form is completed/submitted. A separate pharmacy enrollment is not required.

Indicates Required Field

Healthcare Setting Information

Healthcare Setting Name*:		
Healthcare Setting Address 1*:	Address Line 2:	
City*:	State*:	ZIP*:
Healthcare Setting Telephone Number*:	Healthcare Setting Website URL:	
DEA License Number* (associated with the Healthcare Setting address):	Name of DEA License Holder (if different from Healthcare Setting Name):	DEA License Expiration Date (MM/DD/YYYY)*:

Healthcare Setting Type*: (select all that apply)
☐ Hospital-Emergency Department ☐ Hospital-Inpatient ☐ Mental Health Facility
☐ Other:_____

Your healthcare setting information will be shared with Janssen's patient support and distribution partners, to allow your healthcare setting to purchase product.

Your healthcare setting information (name, location, and phone number) will be listed on a location finder, as a certified healthcare setting, available to healthcare professionals and patients seeking treatment with SPRAVATO®. **If you do not want your information listed, please call SPRAVATO® REMS at 1-855-382-6022.**

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

SPRAVATO® REMS

Inpatient Healthcare Setting Enrollment Form

** Indicates Required Field*

Healthcare Setting and Pharmacy Authorized Representative Information

First Name*:	MI:	Last Name*:

Credentials*: ☐ Physician ☐ Physician Assistant ☐ Nurse ☐ Pharmacist ☐ Other: _____

Telephone Number*:	EXT:	Fax*:	Email Address*:

Healthcare Setting and Pharmacy Alternate Contact

First Name:	Last Name:

Telephone Number:	EXT:	Fax:	Email Address:

Healthcare Setting and Pharmacy Authorized Representative Agreement

I am the Authorized Representative designated by my Healthcare Setting to oversee implementation and coordinate the activities of the SPRAVATO® REMS. By signing this form, I agree, on behalf of myself and my Healthcare Setting, to comply with all REMS requirements:

I will:

- Review the SPRAVATO® Prescribing Information and REMS Program Overview.
- Enroll in the SPRAVATO® REMS by completing this form *and* submitting this form to the SPRAVATO® REMS.
- Have a prescriber onsite during SPRAVATO® administration and monitoring.
- Have a healthcare provider(s) onsite to monitor each patient for at least 2 hours following administration of SPRAVATO® for resolution of sedation and dissociation, and changes in vital signs.
- **Establish processes and procedures** and **train** all relevant staff involved in prescribing, dispensing, and administering SPRAVATO® to ensure that the following takes place in my Healthcare Setting:
  - A healthcare provider counsels the patient prior to receiving SPRAVATO® on the need for monitoring due to risks of sedation and dissociation, changes in vital signs, and the need to have arrangements to safely leave the healthcare setting and not engage in potentially hazardous activities.
  - The patient administers SPRAVATO® under the direct supervision of a healthcare provider.
  - A healthcare provider monitors every patient for at least 2 hours for resolution of sedation and dissociation and changes in vital signs after every dose.
  - SPRAVATO® is not dispensed for use outside the Healthcare Setting.
  - If the authorized representative changes, have the new authorized representative re-certify the Inpatient Healthcare Setting into the REMS by completing the *Inpatient Healthcare Setting Enrollment Form*.
  - Not distribute, transfer, loan, or sell SPRAVATO®.
- Maintain records documenting staff's completion of training.
- Maintain records that all processes and procedures are in place and are being followed.
- Maintain records of all shipments of SPRAVATO® received and dispensing information including the patient name, dose, number of devices, and date administered.
- Comply with audits carried out by Janssen Pharmaceuticals, Inc., or a third party acting on behalf of Janssen Pharmaceuticals, Inc., to ensure that all processes and procedures are in place and are being followed.

Name (please print):

Authorized Representative Signature*:	**Date*:**

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Reference ID: 4913334

SPRAVATO® REMS
Patient Enrollment Form - Outpatient Use Only

INSTRUCTIONS:

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments

1. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091

This section is to be completed by the Prescriber

**** Indicates required field***

Healthcare Setting Information

Healthcare Setting Name*:		
Healthcare Setting DEA License Number* (associated with the Healthcare Setting address):		
Address 1*:	Address 2:	
City*:	State*:	ZIP*:
Phone*:	Fax*:	

Prescriber Information

First Name*:	Last Name*:	
Credentials*: ☐ Physician ☐ Physician Assistant ☐ Nurse ☐ Pharmacist ☐ Other _____ **Specialty*:** ☐ Psychiatry ☐ Internal Medicine ☐ Family Practice ☐ Other_____		Prescriber DEA License Number*:
Phone*:	Fax:	Email*:
Prescriber Signature*:		**Date*:**

Referring Healthcare Provider – if different from Prescriber

First Name:	Last Name:

Relevant Clinical Information

Has the patient previously been treated with ketamine or esketamine for major depressive disorder, treatment-resistant depression, pain syndromes, or any other condition?*	☐ Yes ☐ No

If YES, list all pre-existing conditions treated with ketamine or esketamine:

_____

_____

List all pre-existing medical and psychiatric conditions*:

_____

_____

List concomitant medications (e.g., adjunctive depression medications, sedative hypnotics, psychostimulants, monoamine oxidase inhibitors [MAOIs])*:

_____

_____

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSEN or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

SPRAVATO® REMS

Patient Enrollment Form - Outpatient Use Only

This section is to be completed by the Patient

Your healthcare provider will help you complete this form and provide you with a copy.

**** Indicates required field***

Patient Information

First Name*:	MI:	Last Name*:	Birthdate*: (MM/DD/YYYY):	Sex*: ☐ Male ☐ Female ☐ Other

Email*: (Email is required for online enrollment only)	Phone Number*:
Address 1*:	Address 2:

City*:	State*:	ZIP*:

Patient Agreement

By signing this form, I understand and acknowledge that:

Before my treatment begins, I will:

- Enroll in the SPRAVATO® REMS by completing this *Patient Enrollment Form* with my healthcare provider. Enrollment information will be submitted to the SPRAVATO® REMS.
- Receive counseling on safety risks and the need for monitoring to observe for resolution of sedation and dissociation, and for any changes in vital signs.

During treatment, and after administration I will:

- Use the SPRAVATO® nasal spray myself under the direct observation of a healthcare provider.
- Be observed at the healthcare setting where I get SPRAVATO® for at least 2 hours after each treatment until the healthcare provider determines I am ready to leave the healthcare setting.

I understand:

- Sedation and dissociation can result from treatment with SPRAVATO® and I must stay after each treatment.
  Until these effects resolve, I may feel:
  - sleepy and/or
  - disconnected from myself, my thoughts, feelings and things around me.
- I should make arrangements to safely get home.
- I should not drive or use heavy machinery for the rest of the day on which I receive SPRAVATO®.
- I should contact my doctor or inform him/her at my next visit if I believe I have a side effect or reaction from SPRAVATO®.
- In order to receive SPRAVATO® as an outpatient, I am required to be enrolled in the REMS, and my information will be stored in a database of all outpatients who receive SPRAVATO® in the United States.
- Janssen Pharmaceuticals, Inc. and its agents, including trusted vendors, may contact me or my prescriber via phone, mail, fax, or email to support administration of the REMS.
- Janssen Pharmaceuticals, Inc. and its agents, including trusted vendors, may use, disclose, and share my personal health information for the purpose of the operations of the REMS, including enrolling me into the REMS and administering the REMS, coordinating the dispensing of SPRAVATO®, and releasing and disclosing my personal health information to the Food and Drug Administration (FDA), as necessary, and as otherwise required by law.

Patient Name (please print):	
Patient Signature*:	**Date*:**

Reference ID: 4913334

SPRAVATO® REMS
Pharmacy Enrollment Form

INSTRUCTIONS:

1. Review the *SPRAVATO® Prescribing Information* and the *SPRAVATO® REMS Program Overview*
2. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091

If you are an Inpatient Pharmacy (support inpatient units, emergency department, etc.) and operate under the same DEA license and physical location with your Inpatient Healthcare Setting, your pharmacy will be considered certified once the Inpatient Healthcare Setting Enrollment form is completed/submitted, and you do not require a separate pharmacy enrollment form. This form is intended only for pharmacies that dispense to outpatient facilities.

Indicates Required Field

Pharmacy Information

Name of Pharmacy*:		
Pharmacy Address 1*:	Address Line 2:	
City*:	State*:	ZIP*:
Pharmacy Telephone Number*:	DEA License Number* (On file with distributor account)	DEA Expiration Date* (MM/DD/YYYY):
Pharmacy Type*(select all that apply) ☐ Community/Retail ☐ Specialty ☐ Other:_____		

Your pharmacy information will be shared with Janssen's patient support and distribution partners, to allow your pharmacy to purchase product.

Pharmacy Shipping Address, if different from above

Pharmacy Address (address must match the DEA address associated with your Pharmacy's DEA License Number):	Address Line 2:	
City:	State:	ZIP:

Pharmacy Authorized Representative Information

First Name*:		Last Name*:	Title*:
Telephone Number*:	Ext:	Fax*:	Email Address*:

Pharmacy Alternate Contact

First Name:		Last Name:	
Telephone Number:	Ext:	Fax:	Email Address:

Pharmacy Authorized Representative Agreement

I am the Authorized Representative designated by my pharmacy to carry out the certification process and oversee implementation and coordinate the activities of the SPRAVATO® REMS. By completing this form, I agree, on behalf of the pharmacy, to comply with all REMS requirements:

I will:

- Review the SPRAVATO® Prescribing Information and REMS Program Overview.
- Enroll in the SPRAVATO® REMS by completing this *Pharmacy Enrollment Form* and submitting this form to the SPRAVATO® REMS.
- **Establish processes and procedures** and **train** all relevant staff involved in dispensing SPRAVATO® on the following:
  - SPRAVATO® can only be dispensed to a certified healthcare setting.
  - SPRAVATO® must never be dispensed directly to a patient for home use.
  - Before dispensing SPRAVATO®, verify the healthcare setting is certified.
  - Not distribute, transfer, loan, or sell SPRAVATO® except to certified dispensers.
  - If the authorized representative changes, have the new authorized representative re-certify the Pharmacy into the REMS by completing the *Pharmacy Enrollment Form*.
- Maintain records documenting staff's completion of training.
- Maintain records that all REMS processes and procedures are in place and are being followed.
- Maintain records of all shipments of SPRAVATO® received and dispensing information including patient name, dose, number of devices, and date dispensed.
- Comply with audits carried out by Janssen Pharmaceuticals, Inc., or third party acting on behalf of Janssen Pharmaceuticals, Inc., to ensure that all processes and procedures are in place and are being followed.

Authorized Representative Signature*:	**Date:**

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Phone: 1-855-382-6022 **www.SPRAVATOrems.com** **Fax: 1-877-778-0091**

SPRAVATO® REMS Program Overview
(Risk Evaluation and Mitigation Strategy)

This overview describes the SPRAVATO® REMS requirements and responsibilities of inpatient healthcare settings, outpatient healthcare settings, pharmacies, and patients.

If you have any questions regarding the SPRAVATO® REMS, please visit www.SPRAVATOrems.com or call 1-855-382-6022

Spravato® (esketamine) C III nasal spray

Reference ID:

Reference ID: 4913334

Table of contents

What is the SPRAVATO® REMS (Risk Evaluation and Mitigation Strategy)?

A REMS is a strategy to manage known or potential risks associated with a drug and is required by the U.S. Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

SPRAVATO® is available only through a restricted distribution program called the SPRAVATO® REMS because of the risks of serious adverse outcomes resulting from sedation and dissociation caused by SPRAVATO® administration, and abuse and misuse of SPRAVATO®. SPRAVATO® is intended for use only in a certified Healthcare Setting.

SPRAVATO® is intended for patient administration under the direct observation of a healthcare provider, and patients are required to be monitored by a healthcare provider for at least 2 hours. SPRAVATO® must never be dispensed directly to a patient for home use.

Spravato® (esketamine) C III nasal spray

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How does the SPRAVATO® REMS work?

	Before Prescribing/ Dispensing SPRAVATO®	Before Starting SPRAVATO® for each Patient	During SPRAVATO® Treatment
INPATIENT HEALTHCARE SETTING	Inpatient Healthcare Setting Certification *[covers hospital inpatient, inpatient pharmacy, and emergency departments]*	**Counsel** the patient on the risks and need for monitoring for resolution of sedation and dissociation, and changes in vital signs.	**Supervise** patient administration of SPRAVATO®. **Monitor** each patient for at least 2 hours following administration of SPRAVATO® for resolution of sedation and dissociation, and changes in vital signs. **Report** all suspected adverse events to the SPRAVATO® REMS.
OUTPATIENT HEALTHCARE SETTING	Outpatient Healthcare Setting Certification *[covers outpatient medical offices and clinics]*	**Counsel** the patient on the risks and need for monitoring for resolution of sedation and dissociation, and changes in vital signs. **Enroll** the patient using the ***Patient Enrollment Form***.	**Supervise** patient administration of SPRAVATO®. **Monitor** each patient for at least 2 hours following administration of SPRAVATO® for resolution of sedation and dissociation, and changes in vital signs. **Submit** the ***Patient Monitoring Form***
PHARMACY	Pharmacy Certification *[covers community, retail, and specialty pharmacies]*	**Verify** that the healthcare setting is certified through the processes and procedures established as a requirement of the SPRAVATO® REMS.	
PATIENT		**Receive counseling** from a healthcare provider on the need for monitoring for resolution of sedation and dissociation, and changes in vital signs. Outpatient Enrollment	**Administer SPRAVATO®** under the direct supervision of a healthcare provider. **Be observed** for at least 2 hours after each treatment of SPRAVATO® for resolution of sedation and dissociation, and changes in vital signs at the healthcare setting.

What are the Requirements of the SPRAVATO® REMS?

- In order for patients to receive SPRAVATO®, healthcare settings, pharmacies, and patients must comply with all requirements of the SPRAVATO® REMS

INPATIENT HEALTHCARE SETTING REQUIREMENTS

Become Certified*:

1. **Designate** an Authorized Representative to oversee implementation and coordinate the activities of the SPRAVATO® REMS
2. **Review** the following materials:
   - SPRAVATO® Prescribing Information
   - SPRAVATO® REMS Program Overview (this document)
3. Have the Authorized Representative **complete** and **submit** the ***Inpatient Healthcare Setting Enrollment Form*** at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091
4. Once submitted, you will be notified of certification in the SPRAVATO® REMS and you will receive information on additional requirements necessary to order and receive SPRAVATO®

Before treating a patient:

1. **Establish** processes and procedures and train all relevant staff involved in prescribing, dispensing, and administering SPRAVATO®
2. Have a healthcare provider **counsel** the patient prior to receiving SPRAVATO® on the need for monitoring due to risks of sedation and dissociation, changes in vital signs, and the need to have arrangements to safely leave the healthcare setting and not engage in potentially hazardous activities.

*As an Inpatient Healthcare Setting (with inpatient units, emergency department, etc.), your Inpatient Pharmacy, operating under the same Drug Enforcement Administration (DEA) license and physical location, will be considered certified once the ***Inpatient Healthcare Setting Enrollment Form*** is completed/submitted. **A separate pharmacy enrollment is not required**.

At All Times:

1. **Ensure** relevant staff are trained and follow all established processes and procedures to comply with SPRAVATO® REMS requirements†
2. **Have a prescriber onsite** during SPRAVATO® administration and monitoring
3. **Have a healthcare provider monitor** every patient for at least 2 hours for resolution of sedation and dissociation and changes in vital signs after every dose
4. **Ensure** SPRAVATO® is not dispensed for use outside the Healthcare Setting
5. **Maintain** records documenting staff completion of training
6. **Maintain** records of all shipments of SPRAVATO® received and dispensing information including the patient name, dose, number of devices, and date administered
7. **Comply** with audits carried out by Janssen Pharmaceuticals, Inc. or third party acting on behalf of Janssen Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed

† To review all SPRAVATO® REMS Inpatient Healthcare Setting requirements see the ***Inpatient Healthcare Setting Enrollment Form***

OUTPATIENT HEALTHCARE SETTING REQUIREMENTS

Become Certified:

1. **Designate** an Authorized Representative to oversee implementation and coordinate the activities of the SPRAVATO® REMS
2. **Review** the following materials:
   - SPRAVATO® Prescribing Information
   - SPRAVATO® REMS Program Overview (this document)
3. Have the Authorized Representative **complete** and **submit** the ***Outpatient Healthcare Setting Enrollment Form*** at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091.
4. Once submitted, you will be notified of certification in the SPRAVATO® REMS and you will receive information on additional requirements necessary to order and receive SPRAVATO®

Before treating a patient:

1. **Establish** processes and procedures and train all relevant staff involved in prescribing, dispensing, and administering SPRAVATO® to comply with all SPRAVATO® REMS requirements
2. Have a healthcare provider **counsel** the patient prior to receiving SPRAVATO® on the need for enrollment, monitoring, risks of sedation and dissociation, and changes in vital signs
3. Have a prescriber **enroll** the patient by completing and submitting the ***Patient Enrollment Form*** to the SPRAVATO® REMS
4. **Verify** the patient is enrolled in the SPRAVATO® REMS before dispensing SPRAVATO® for patient administration

At All Times:

1. **Ensure** relevant staff are trained and follow all established processes and procedures to comply with all SPRAVATO® REMS requirements*
2. Have a **prescriber onsite** during SPRAVATO® administration and monitoring
3. Have the patient **administer** SPRAVATO® under the direct supervision of a healthcare provider
4. Have a **healthcare provider(s) onsite** to monitor each patient for at least 2 hours following administration of SPRAVATO® for resolution of sedation and dissociation, and changes in vital signs after every dose
5. **Document** and **submit** a ***Patient Monitoring Form*** for every patient within 7 days following administration of every dose of SPRAVATO®
6. **Notify** the SPRAVATO® REMS in advance if patient treatment will be transferred from one REMS-certified Healthcare Setting to another REMS-certified Healthcare Setting
7. **Ensure** SPRAVATO® is not dispensed for use outside the Healthcare Setting
8. **Maintain** records documenting staff completion of training
9. **Maintain** records of all shipments of SPRAVATO® received and dispensing information including the patient name, dose, number of devices, and date administered
10. **Comply** with audits carried out by Janssen Pharmaceuticals, Inc. or third party acting on behalf of Janssen Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed

*To review all SPRAVATO® REMS Outpatient Healthcare Setting requirements see the ***Outpatient Healthcare Setting Enrollment Form***

Reference ID: 4913334

PHARMACY REQUIREMENTS - FOR OUTPATIENT DISPENSING ONLY

Become Certified:

1. **Designate** an Authorized Representative to oversee implementation and coordinate the activities of the SPRAVATO® REMS
2. **Review** the following materials:
   - SPRAVATO® Prescribing Information
   - SPRAVATO® REMS Program Overview (this document)
3. Have the Authorized Representative **complete** and **submit** the ***Pharmacy Enrollment Form*** at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091
4. Once submitted, you will be notified of certification in the SPRAVATO® REMS and you will receive information on additional requirements necessary to order and receive SPRAVATO®

Before Dispensing:

1. **Establish** processes and procedures and train all relevant staff involved in dispensing SPRAVATO® to comply with all SPRAVATO® REMS requirements
2. **Verify** the healthcare setting is certified before dispensing SPRAVATO®

At All Times:

1. **Ensure** relevant staff are trained and follow all established processes and procedures to comply with all SPRAVATO® REMS requirements*
2. **Ensure** SPRAVATO® is never dispensed directly to a patient for home use
3 **Ensure** SPRAVATO® is only dispensed to a certified healthcare setting
4. **Maintain** records documenting staff's completion of training
5. **Maintain** records of all shipments of SPRAVATO® received and dispensing information including the patient name, dose, number of devices, and date dispensed
6. **Comply** with audits carried out by Janssen Pharmaceuticals, Inc. or third party acting on behalf of Janssen Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed

*To review all SPRAVATO® REMS Pharmacy requirements see the ***Pharmacy Enrollment Form***

PATIENT REQUIREMENTS

Before Treatment:

1. **Receive** counseling from a healthcare provider on risks and the need for monitoring for resolution of sedation and dissociation, and changes in vital signs
2. **Outpatient Only:**

   Enroll in the SPRAVATO® REMS Program by completing the ***Patient Enrollment Form*** with a healthcare provider. Enrollment information will be provided to the SPRAVATO® REMS Program

During Treatment:

1. **Administer** SPRAVATO® nasal spray under the direct observation of a healthcare provider
2. **Be observed** at the healthcare setting where SPRAVATO® is received for at least 2 hours after each treatment until the healthcare provider determines the patient is ready to leave the healthcare setting

At All Times*:

1. **Make arrangements** to safely get home after receiving SPRAVATO®, if leaving the healthcare setting
2. **Do not** drive or use heavy machinery for the rest of the day after receiving SPRAVATO®
3. **Contact the healthcare provider** or inform the healthcare provider at the next visit if a side effect or reaction from SPRAVATO® occurs

*To review all SPRAVATO® REMS requirements for patients receiving SPRAVATO® in an Outpatient Healthcare Setting, see the ***Patient Enrollment Form***

SPRAVATO® REMS Resources

INPATIENT HEALTHCARE SETTING	OUTPATIENT HEALTHCARE SETTING	PHARMACY
• *Inpatient Healthcare Setting Enrollment Form* • *REMS Program Overview* • *Prescribing Information*	• *Outpatient Healthcare Setting Enrollment Form* • *Patient Enrollment Form* • *Patient Monitoring Form* • *REMS Program Overview* • *Prescribing Information*	• *Pharmacy Enrollment Form* • *REMS Program Overview* • *Prescribing Information*

Contact the SPRAVATO® REMS

Phone: 1-855-382-6022
Fax: 1-877-778-0091
Hours of Operation: Monday- Friday 8:00 AM - 8:00 PM ET
Visit www.SPRAVATOrems.com

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Please see the Prescribing Information for more information.

Spravato® (esketamine) CIII nasal spray

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Spravato® (esketamine) nasal spray

SPRAVATO® REMS

Patient Monitoring Form - Outpatient Use Only

For Healthcare Setting Use Place Patient Label or Barcode Here

INSTRUCTIONS:

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments.

1. Complete all required fields on this form after **every** treatment session for **all outpatients** enrolled in the SPRAVATO® REMS.
2. Submit completed patient monitoring forms within **7 days**, online at www.SPRAVATOrems.com or by fax (1-877-778-0091).

Indicates Required Field

Patient Information (PRINT)

First Name*:	MI:	Last Name*:	Birthdate* (MM/DD/YYYY):	Sex*: ☐ Male ☐ Female ☐ Other

Concomitant Medication

Is the patient currently taking any of the following medication(s) that may cause sedation or blood pressure changes?

- Benzodiazepines* ☐ Yes ☐ No
- Non-benzodiazepine sedative hypnotics* ☐ Yes ☐ No
- Psychostimulants* ☐ Yes ☐ No
- Monoamine oxidase inhibitors (MAOIs)* ☐ Yes ☐ No

Healthcare Provider Conducting Patient Monitoring (PRINT)

First Name*:	Last Name*:
Telephone*:	Email*:

Healthcare Setting Information (PRINT)

Healthcare Setting Name*:		
Healthcare Setting Address 1*:	Healthcare Setting Address 2:	
City*:	State*:	ZIP*:

Patient Treatment Session Information (Administration and Monitoring)

Treatment Date*	Date (MM/DD/YYYY): _____		
Dose Administered*	☐ 56 mg ☐ 84 mg ☐ Other:_____	**Lot Number*:** _____	
Treatment Duration*	Total time _____**minutes** (from 1st device administration to completion of monitoring) **Patient must be monitored for at least 2 hours**		
REMS Evaluation Question*	*If there was not a 2-hour minimum monitoring requirement, when would this patient have been ready to leave/no longer require monitoring?* _____ ***minutes*** *from start of administration*		
Monitoring of Vital Signs*	Vital signs were in acceptable range **prior** to: • administration? ☐ Yes ☐ No • treatment session completion? ☐ Yes ☐ No		
Monitoring of Blood Pressure*	**Prior to administration** _____/_____ mmHg	**40 mins post-administration** _____/_____ mmHg	**Prior to treatment session completion** _____/_____ mmHg

Did the patient experience Sedation and/or Dissociation

Sedation*: ☐ Yes ☐ No	**Dissociation***: ☐ Yes ☐ No
Onset of symptoms from start of administration* ☐ 1-29 mins ☐ 30-59 mins ☐ 60-89 mins ☐ 90-120 mins ☐ >120 mins	**Onset of symptoms** from start of administration* ☐ 1-29 mins ☐ 30-59 mins ☐ 60-89 mins ☐ 90-120 mins ☐ >120 mins
Resolution of symptoms within 2 hours?* ☐ Yes ☐ No Specify total time to resolution*: _____minutes	**Resolution of symptoms** within 2 hours?* ☐ Yes ☐ No Specify total time to resolution*: _____minutes
Medication(s) given for sedation?* ☐ Yes ☐ No •If YES, name and dose of medication(s): _____	**Medication(s) given for dissociation?*** ☐ Yes ☐ No •If YES, name and dose of medication(s): _____

Spravato® (esketamine) CIII nasal spray

SPRAVATO® REMS

Patient Monitoring Form - Outpatient Use Only

For Healthcare Setting Use Place Patient Label or Barcode Here

*** Indicates Required Field**

Patient Information (PRINT)

First Name*:	MI:	Last Name*:	Birthdate* (MM/DD/YYYY):	Sex*: ☐ Male ☐ Female ☐ Other

Healthcare Provider Conducting Patient Monitoring (PRINT)

First Name*:	Last Name*:
Phone*:	Email:
Treatment Date (MM/DD/YYYY):	

Serious Adverse Events (PRINT)

A serious adverse event (SAE) for this SPRAVATO® REMS is defined as any event that results in/is:

- **Hospitalization**
- **Disability or permanent damage**
- **Death**
- **Life-threatening**
- **Important medical event**
  – defined as any event that may jeopardize the patient or may require intervention to prevent one of the above outcomes

*All non-serious adverse events or product quality complaints that are **not defined above**, should be reported to: Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.*

Did the patient experience a serious adverse event?* ☐ **Yes** ☐ **No** **If YES, describe below.**

Event resulted in the following: (check all that apply)	**Event Timing**	**Event Description** (Please list one event per row)	**Event Resolution**
☐ Hospitalization ☐ Disability or permanent damage ☐ Death ☐ Life-threatening ☐ Important Medical Event	☐ During treatment sessions ☐ Between treatment sessions Date of Event ________ (MM/DD/YYYY)		☐ Yes ☐ No ☐ Unknown
☐ Hospitalization ☐ Disability or permanent damage ☐ Death ☐ Life-threatening ☐ Important Medical Event	☐ During treatment sessions ☐ Between treatment sessions Date of Event ________ (MM/DD/YYYY)		☐ Yes ☐ No ☐ Unknown
☐ Hospitalization ☐ Disability or permanent damage ☐ Death ☐ Life-threatening ☐ Important Medical Event	☐ During treatment sessions ☐ Between treatment sessions Date of Event ________ (MM/DD/YYYY)		☐ Yes ☐ No ☐ Unknown

Janssen Pharmaceuticals, Inc., Safety Department may follow up to obtain more information about these events.

SPRAVATO® REMS
(Risk Evaluation and Mitigation Strategy)

What is the SPRAVATO® REMS (Risk Evaluation and Mitigation Strategy)?

A REMS is a strategy to manage known or potential risks associated with a drug and is required by the U.S. Food Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

SPRAVATO® (esketamine) nasal spray CIII is available only through a restricted distribution program called th because of the risks of serious adverse outcomes resulting from sedation and dissociation caused by SPRAVA abuse and misuse of SPRAVATO. SPRAVATO® is intended for use only in a certified Healthcare Setting.

SPRAVATO® is intended for patient administration under the direct observation of a healthcare provider, and be monitored by a healthcare provider for at least 2 hours. SPRAVATO® must never be dispensed directly to a

Program Requirements

Inpatient Healthcare Setting

Inpatient Healthcare Settings must be certified in the SPRAVATO® REMS in order to treat patients with SPRAVATO®

Inpatient Healthcare Setting Certification ▸

Outpatient Healthcare Setting

Outpatient Healthcare Settings must be certified in the SPRAVATO® REMS in order to treat patients with SPRAVATO®

Outpatient Healthcare Setting Certification ▸

Pharmacy

Pharmacies must be certified in the SPRAVATO® REMS in order to dispense SPRAVATO®

Pharmacy Certification ▸

Pati in th orde trea

Inpatient Healthcare Settings

SPRAVATO® REMS Inpatient Healthcare Setting Enrollment

Inpatient Healthcare Settings must be certified in the SPRAVATO® REMS in order to treat patients with

SPRAVATO® is intended for patient administration under the direct observation of a healthcare provider, d adverse outcomes resulting from sedation and dissociation caused by SPRAVATO administration, and ab SPRAVATO. SPRAVATO® is intended for use only in a certified Healthcare Setting.

Inpatient Healthcare Settings are NOT required to enroll patients or submit *Patient Monitoring Forms* to the

As an Inpatient Healthcare Setting (with inpatient units, emergency department, etc.), your Inpatient Pharmac same Drug Enforcement Administration (DEA) license and physical location, will be considered certified once th *Setting Enrollment Form* is completed/submitted. A separate pharmacy enrollment is not re

Inpatient Healthcare Settings are required to report all suspected adverse events to the SPRAVATO® REMS

How does my Inpatient Healthcare Setting become certified i the SPRAVATO® REMS?

1

Step 1: Designate an Authorized Representative to oversee implementation and compliance with the REMS requirements.

2

Step 2: Review the following materials:

- *SPRAVATO® Prescribing Information*
- *SPRAVATO® REMS Program Overview*

Outpatient Healthcare Settings

SPRAVATO® REMS Outpatent Healthcare Setting Enrollment

Outpatient Healthcare Settings must be certified in the SPRAVATO® REMS in order to prescribe pr

SPRAVATO® is intended for patient administration under the direct observation of a healthcare provider, du adverse outcomes resulting from sedation and dissociation caused by SPRAVATO administration, and abu SPRAVATO. SPRAVATO® is intended for use only in a certified Healthcare Setting.

Outpatient Healthcare Settings are required to enroll patients prior to patient treatment and submit *Patient Mo* each patient treatment to the SPRAVATO® REMS.

Outpatient Healthcare Setting Enrollment is intended only for outpatient medical offices and cl Emergency departments within hospitals are certified through the Inpatient Healthcare Setting enr

How does my Outpatient Healthcare Setting become certified in the SPRAVATO® REMS?

1

Step 1: Designate an Authorized Representative to oversee implementation and compliance with the REMS requirements.

2

Step 2: Review the following materials:

- *SPRAVATO® Prescribing Information*
- *SPRAVATO® REMS Program Overview*

Pharmacies

SPRAVATO® REMS Pharmacy Enrollment - for Outpatient Dispensin

Pharmacies must be certified in the SPRAVATO® REMS to be able to receive and dispense SPRA

If you are an Inpatient Pharmacy (support inpatient units, emergency department, etc.) and operate under the physical location with your Inpatient Healthcare Setting, your pharmacy will be considered certified once the Setting Enrollment form is completed/submitted, and you do not require a separate pharmacy enrollmen enrollment is intended only for pharmacies that dispense to outpatient facilities.

How does my Pharmacy become certified in the SPRAVATO® REMS?

1

Step 1: Designate an Authorized Representative to oversee implementation and compliance of the SPRAVATO® REMS requirements.

2

Step 2: Review the following materials:

- *SPRAVATO® Prescribing Information*
- *SPRAVATO® REMS Program Overview*

3

Step 3: Complete and submit the *SPRAVATO® REMS Pharmacy*

Patients

What is the SPRAVATO® REMS (Risk Evaluation and Mitigation Strateg

Because of the risks associated with SPRAVATO®, the Food and Drug Administration (FDA) has required a special
Evaluation and Mitigation Strategy (REMS). As part of the REMS, your healthcare provider will discuss the ris
sedation (feeling sleepy), dissociation (feeling disconnected from yourself, including thoughts, feelings, and thin
on SPRAVATO® with you. Both you and your healthcare provider must sign the *Patient Enrollment Form* for you to
an outpatient medical office or clinic, excluding emergency departments. Your healthcare provider will provide
form to the SPRAVATO® REMS.

How do I enroll in the SPRAVATO® REMS?

**If your healthcare provider and you have both agreed that SPRAVATO® is the appropriate treatment for you, you wi
SPRAVATO® REMS in order to receive treatment with SPRAVATO® in an outpatient medical office or clinic, exclu
departments.**

These are the steps to take in partnership with your healthcare provider:

1

Step 1: Make sure you understand:

A. How to enroll and take part in the SPRAVATO® REMS

B. The benefits and risks of SPRAVATO®

C. That each time you receive SPRAVATO®:

- You will need to use SPRAVATO® Nasal Spray yourself under direct observatio
of a healthcare provider in a healthcare setting, such as an outpatient medic
office or clinic, excluding emergency departments

Contact Us

Contact the SPRAVATO® REMS

Phone: 1-855-382-6022

Fax: 1-877-778-0091

Hours of Operation: Monday — Friday 8:00 AM — 8:00 PM ET

Healthcare providers should report suspected adverse events or product quality complaints associated with SPI
1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medw

For SPRAVATO® REMS Program information contact:

Phone: 1-855-382-6022

Fax: 1-877-778-0091

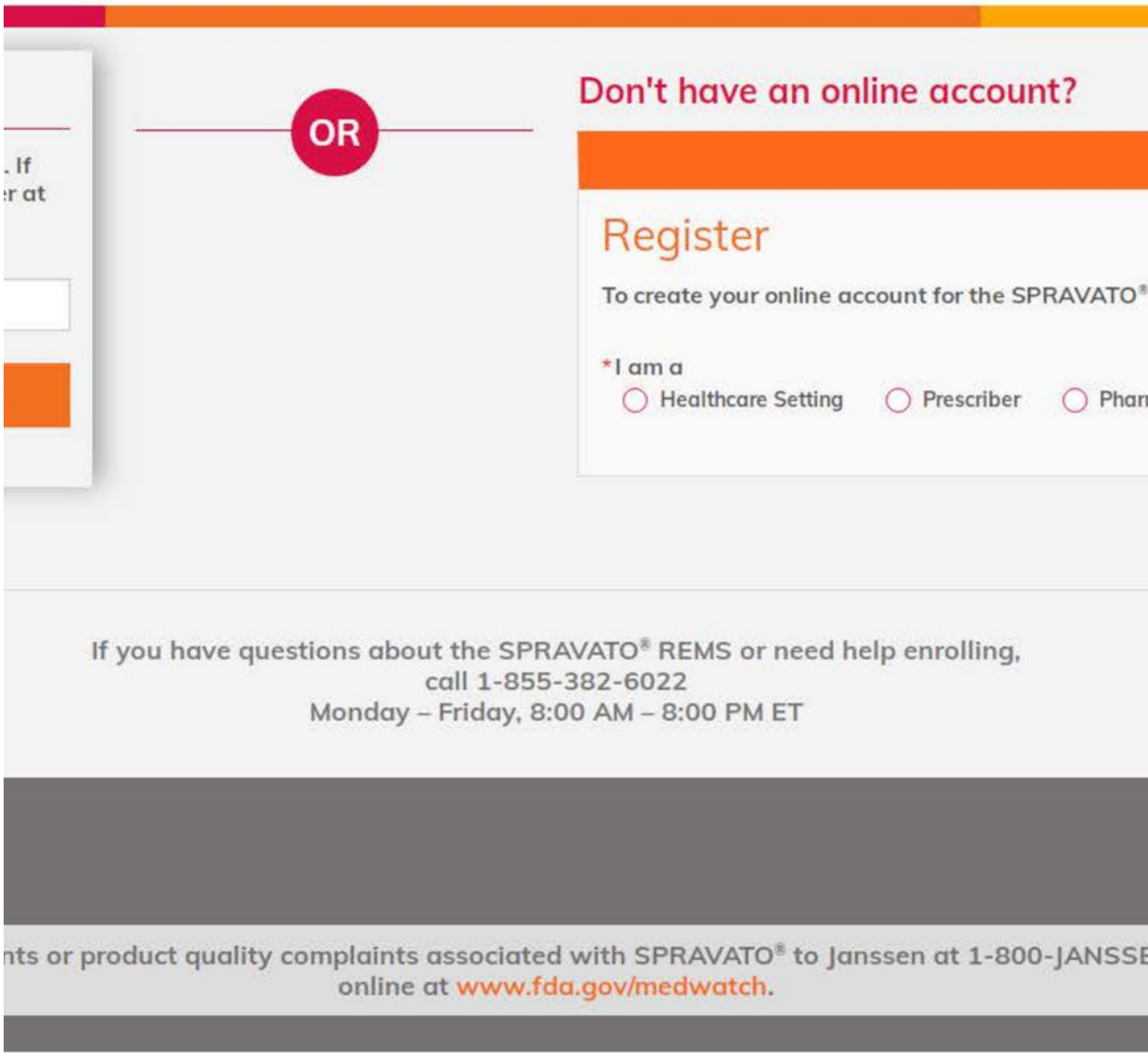
Resources

Inpatient Healthcare Setting Resources for SPRAVATO® REMS

- *SPRAVATO® REMS Inpatient Healthcare Setting Enrollment Form*
- *SPRAVATO® Prescribing Information*
- *SPRAVATO® REMS Program Overview*

Outpatient Healthcare Setting Resources for SPRAVATO® REM

- *SPRAVATO® REMS Outpatient Healthcare Setting Enrollment Form*
- *SPRAVATO® REMS Program Overview*
- *SPRAVATO® REMS Patient Enrollment Form*
- *SPRAVATO® Prescribing Information*
- *SPRAVATO® REMS Patient Monitoring Form*


. If
r at
OR
Don't have an online account?
Register
To create your online account for the SPRAVATO®
*I am a
Healthcare Setting
Prescriber
Phar
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Monday – Friday, 8:00 AM – 8:00 PM ET
nts or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSE
online at www.fda.gov/medwatch.

Spravato® (esketamine) C III
nasal spray

Login

Your username was supplied to you via email when you registered. If you need assistance, please contact the REMS Coordinating Center at 1-855-382-6022.

User Name

Forgot Username

LOGIN

OR

Don't have an online account?

Register

To create your online account for the SPRAVATO

*I am a

Healthcare Setting Prescriber Pha

Healthcare Setting Authorized R

*First Name

*Last Name

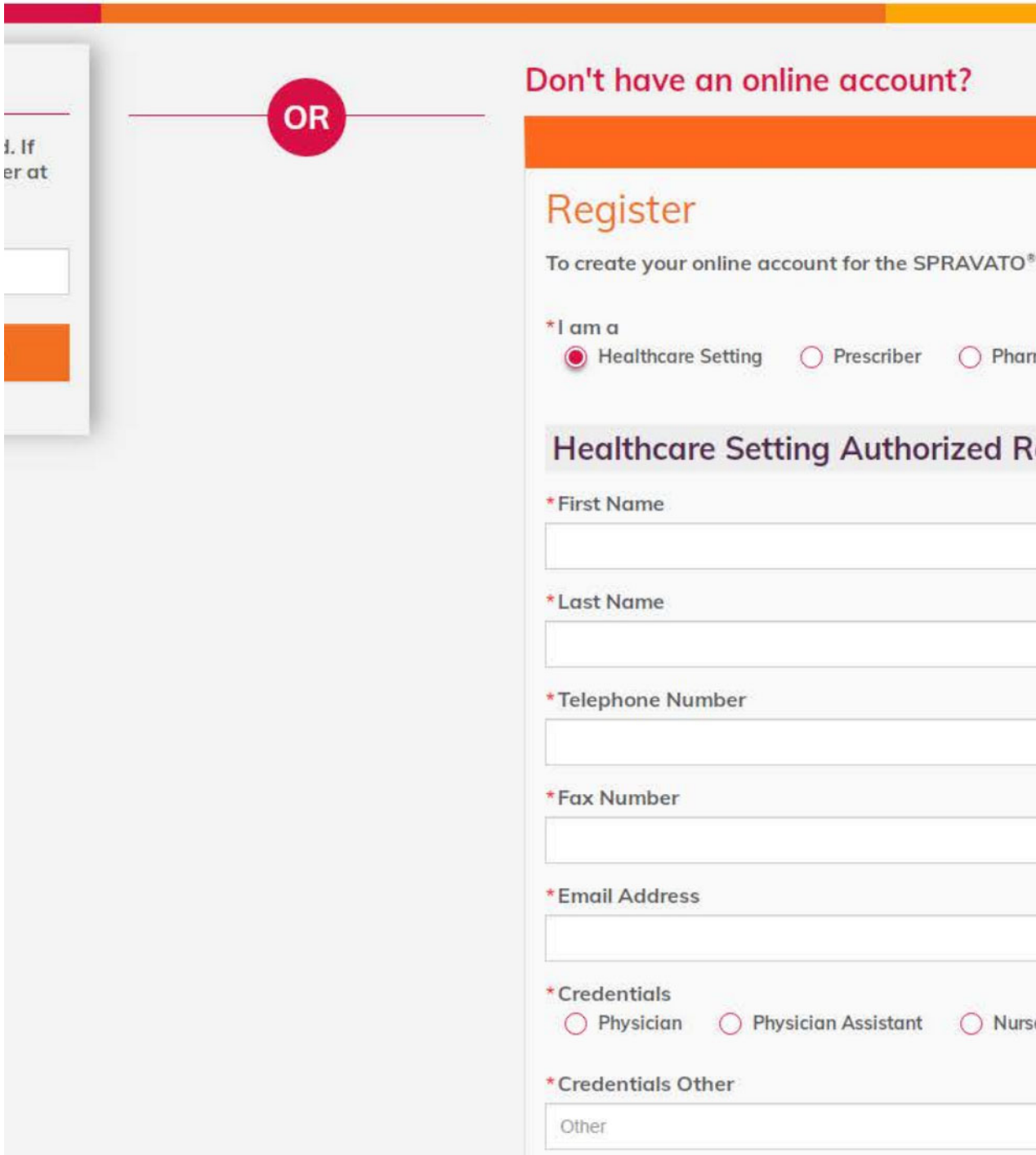
*Telephone Number

*Fax Number

*Email Address

*Credentials

Physician Physician Assistant Nur


OR
Don't have an online account?
Register
To create your online account for the SPRAVATO®
*I am a
Healthcare Setting
Prescriber
Healthcare Setting Authorized R
*First Name
*Last Name
*Telephone Number
*Fax Number
*Email Address
*Credentials
Physician
Physician Assistant
*Credentials Other
Other

Spravato® (esketamine) C III nasal spray

Account Submitted Successfully

Thank you for submitting your information to create your web account for the SPRAVATO® REMS.

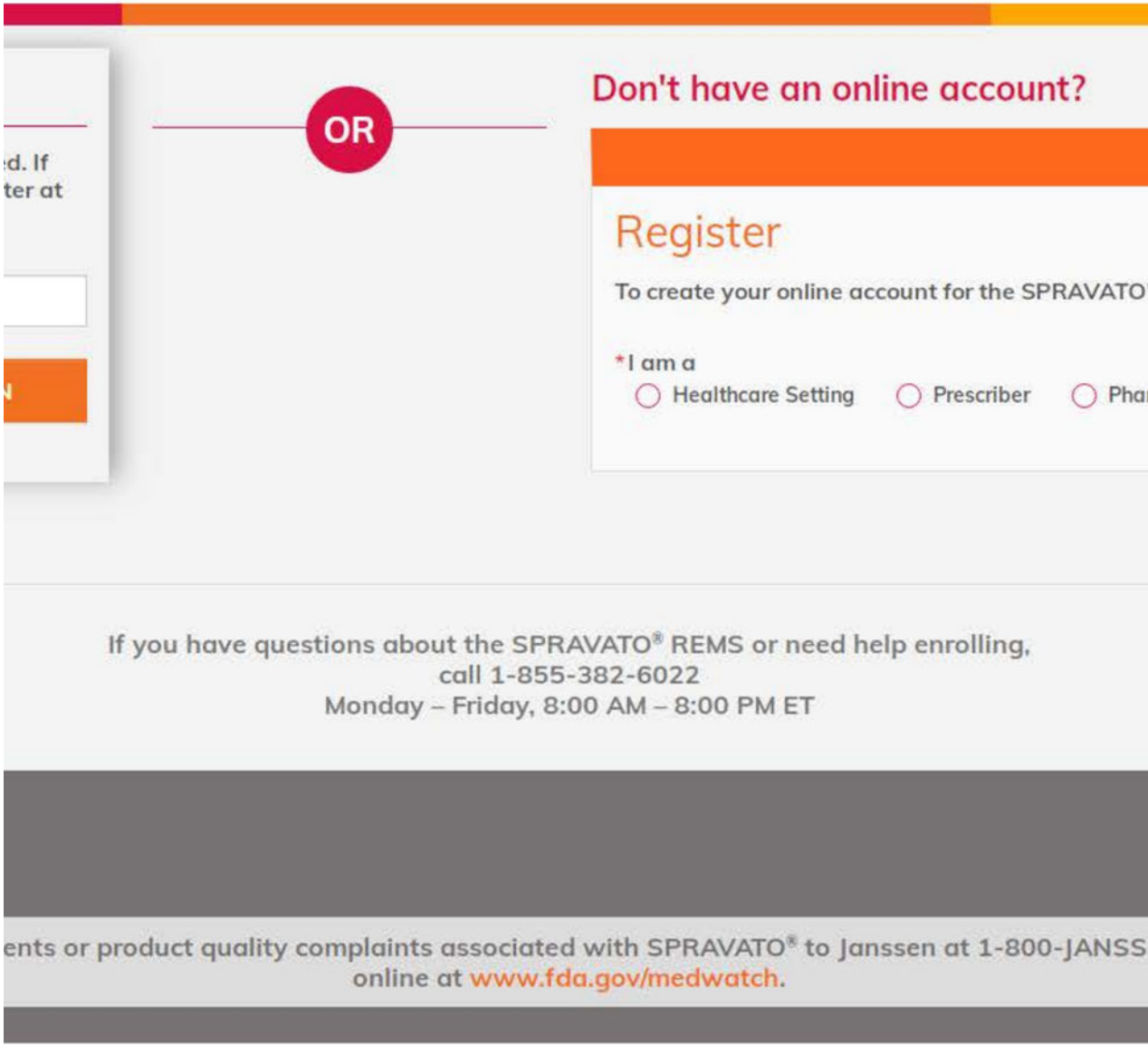
A confirmation of this submission has been sent to the email address provided. You can expect to receive 2 emails, one contains your username and the second contains yo temporary password. Please login with the username provided. You will then be prompted to update your password.

If you do not receive the emails within the next few hours, or would like to update your enrollment information at any time, please contact the SPRAVATO® REMS at 1-855- 6022.

LOGIN

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSS online at www.fda.gov/medwatch.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To create your online account for the SPRAVATO
*I am a
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Prescriber
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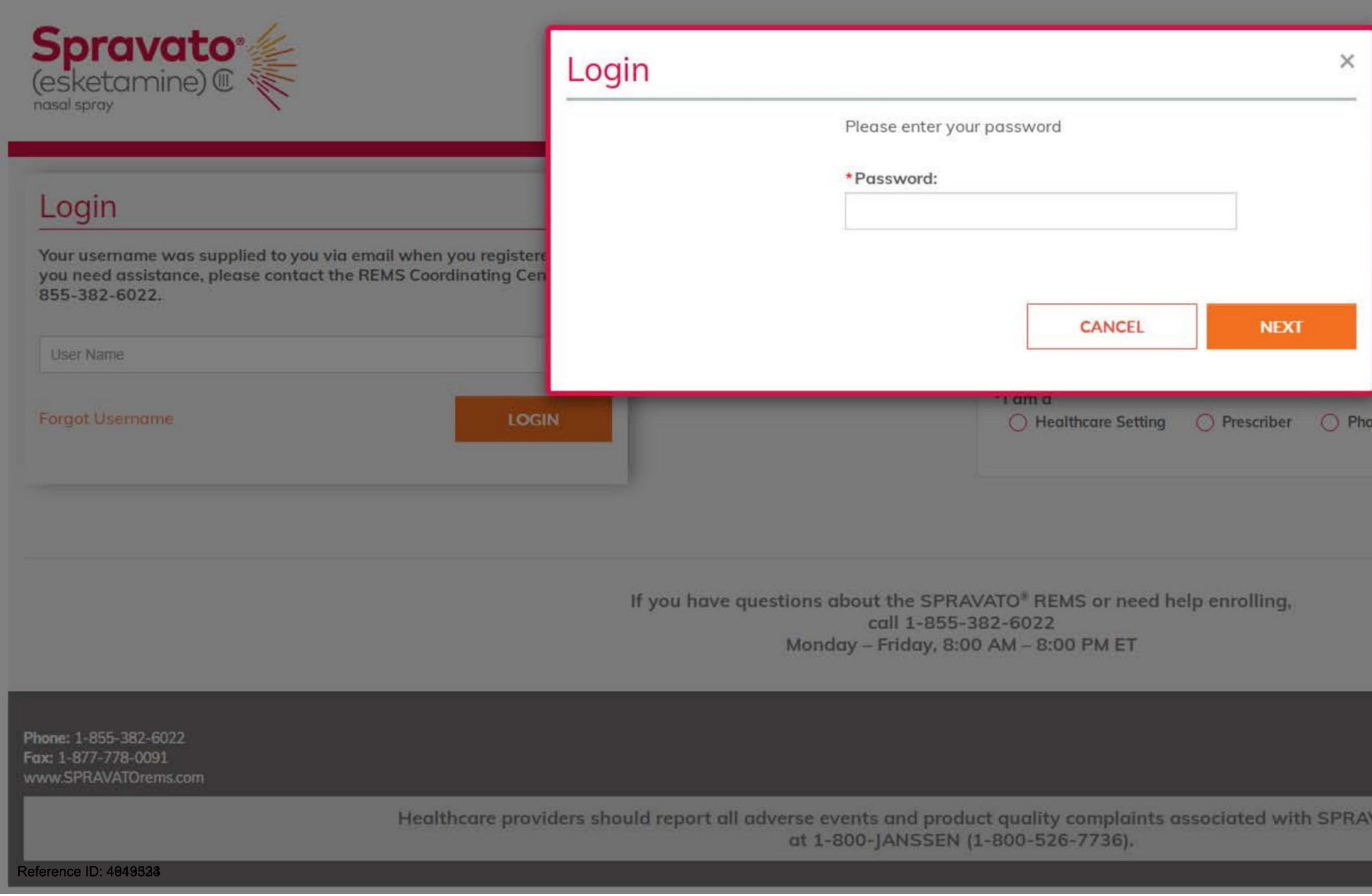
online at www.fda.gov/medwatch.


Spravato®
(esketamine) C-III
nasal spray
Login
Your username was supplied to you via email when you registere
you need assistance, please contact the REMS Coordinating Cen
855-382-6022.
User Name
Forgot Username
LOGIN
Login
Please enter your password
*Password:
CANCEL
NEXT
Healthcare Setting
Prescriber
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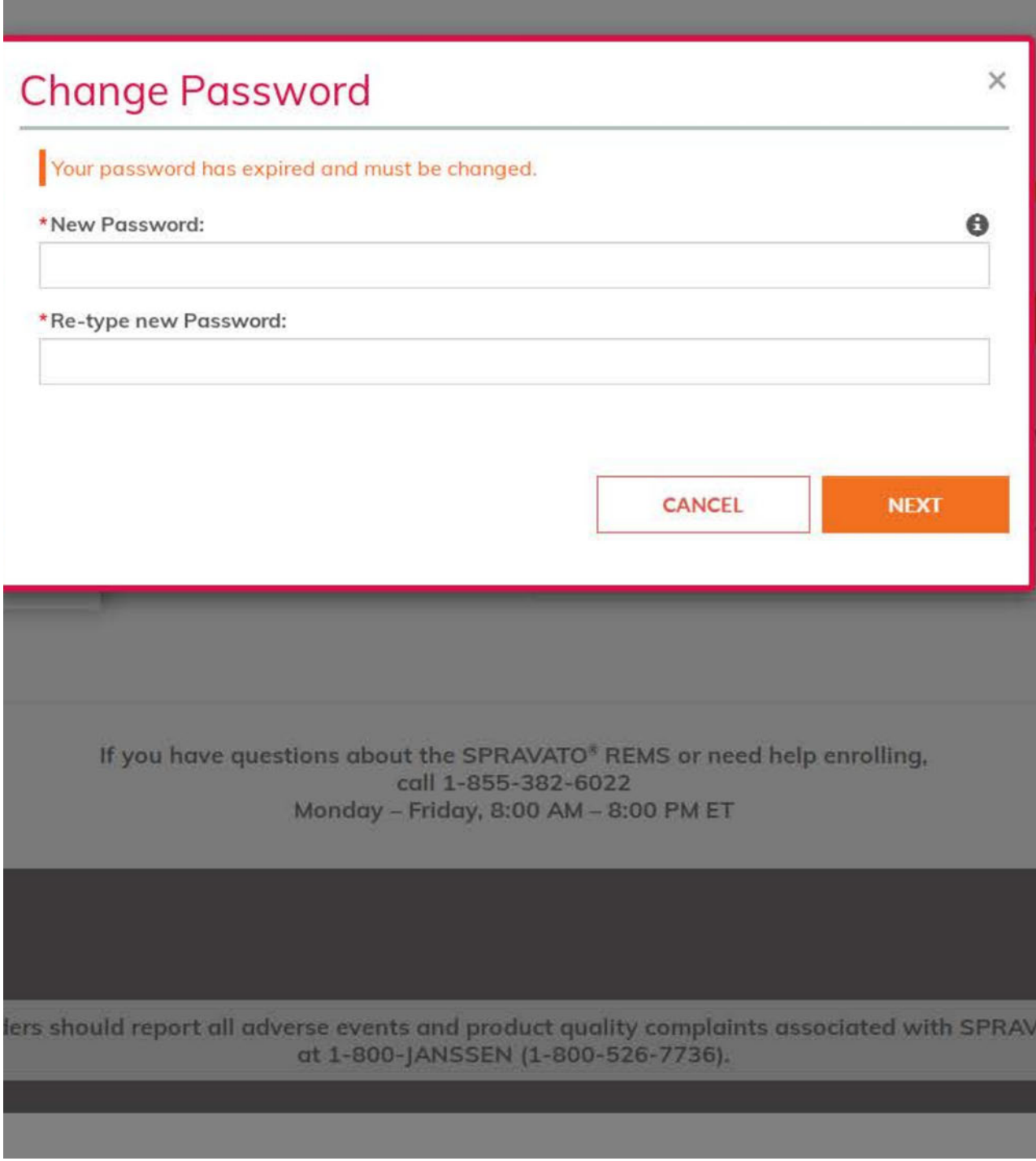
at 1-800-JANSSEN (1-800-526-7736).


Change Password
Your password has expired and must be changed.
*New Password:
*Re-type new Password:
CANCEL
NEXT
If you have questions about the SPRAVATO® REMS or need help enrolling,
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Spravato® (esketamine) C III nasal spray

Login

Your username was supplied to you via email when you registere
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855-382-6022.

User Name

Forgot Username

LOGI

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com

Healthcare provi

Update Profile









*Security Caption:

*Security Question | *Answer

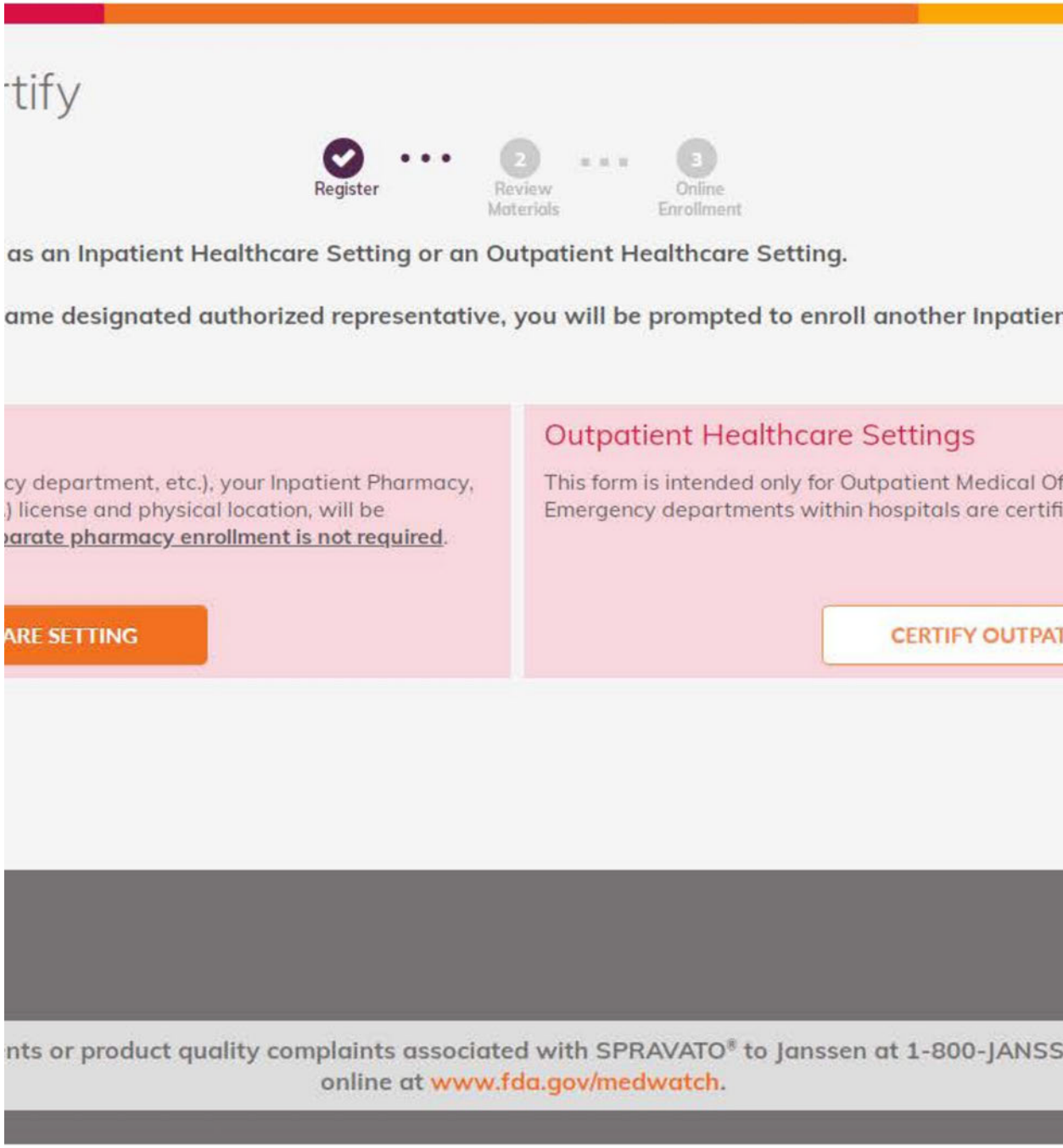
-- Please Select -- | Answer

-- Please Select -- | Answer

-- Please Select -- | Answer

CANCEL NEXT

Reference ID: 4049523


tify
Register
2
Review Materials
3
Online Enrollment
as an Inpatient Healthcare Setting or an Outpatient Healthcare Setting.
ame designated authorized representative, you will be prompted to enroll another Inpatien
cy department, etc.), your Inpatient Pharmacy,
) license and physical location, will be
arate pharmacy enrollment is not required.
ARE SETTING
Outpatient Healthcare Settings
This form is intended only for Outpatient Medical Of
Emergency departments within hospitals are certifi
CERTIFY OUTPAT
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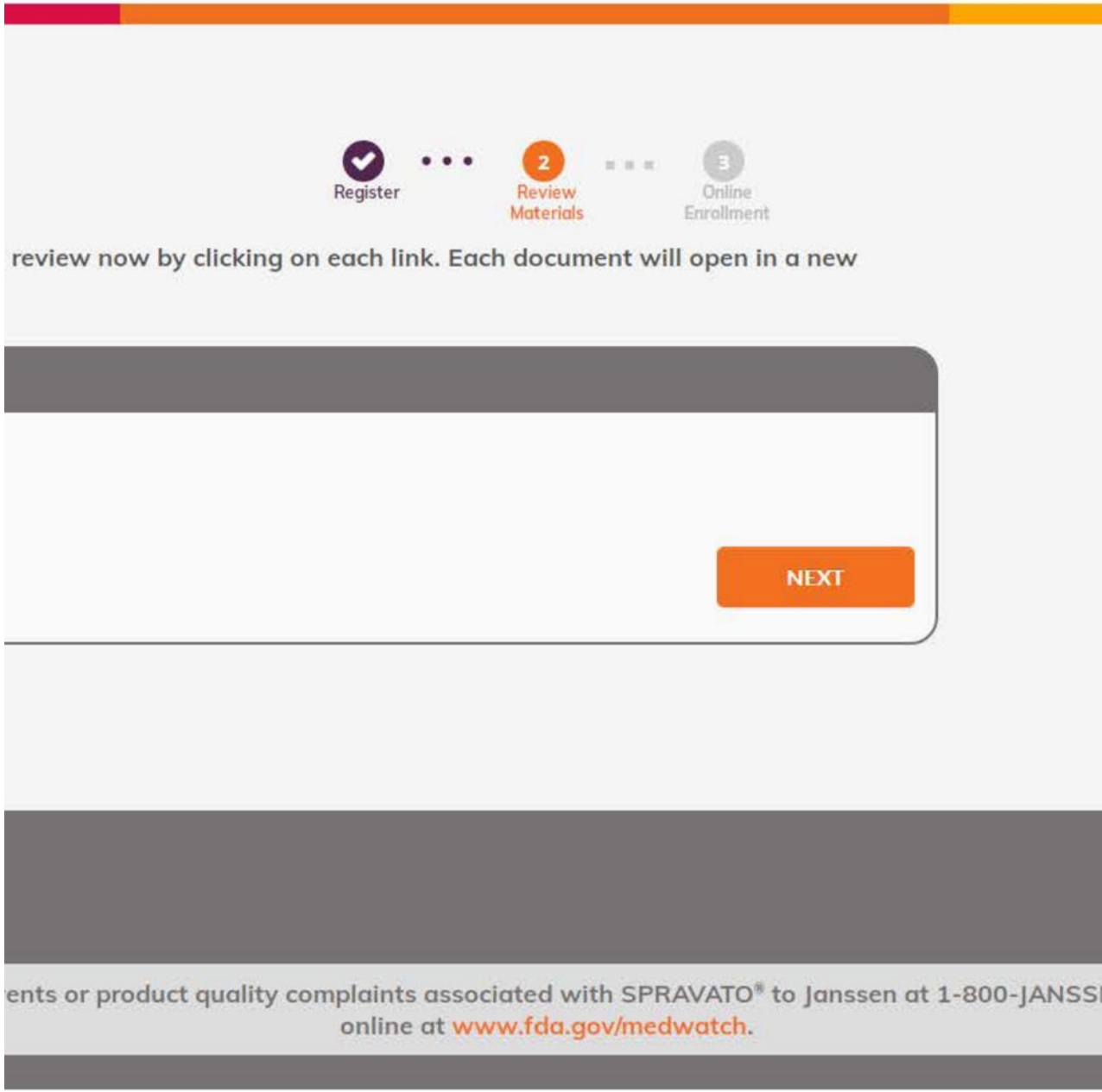
online at www.fda.gov/medwatch.


Register
2
Review Materials
3
Online Enrollment
review now by clicking on each link. Each document will open in a new
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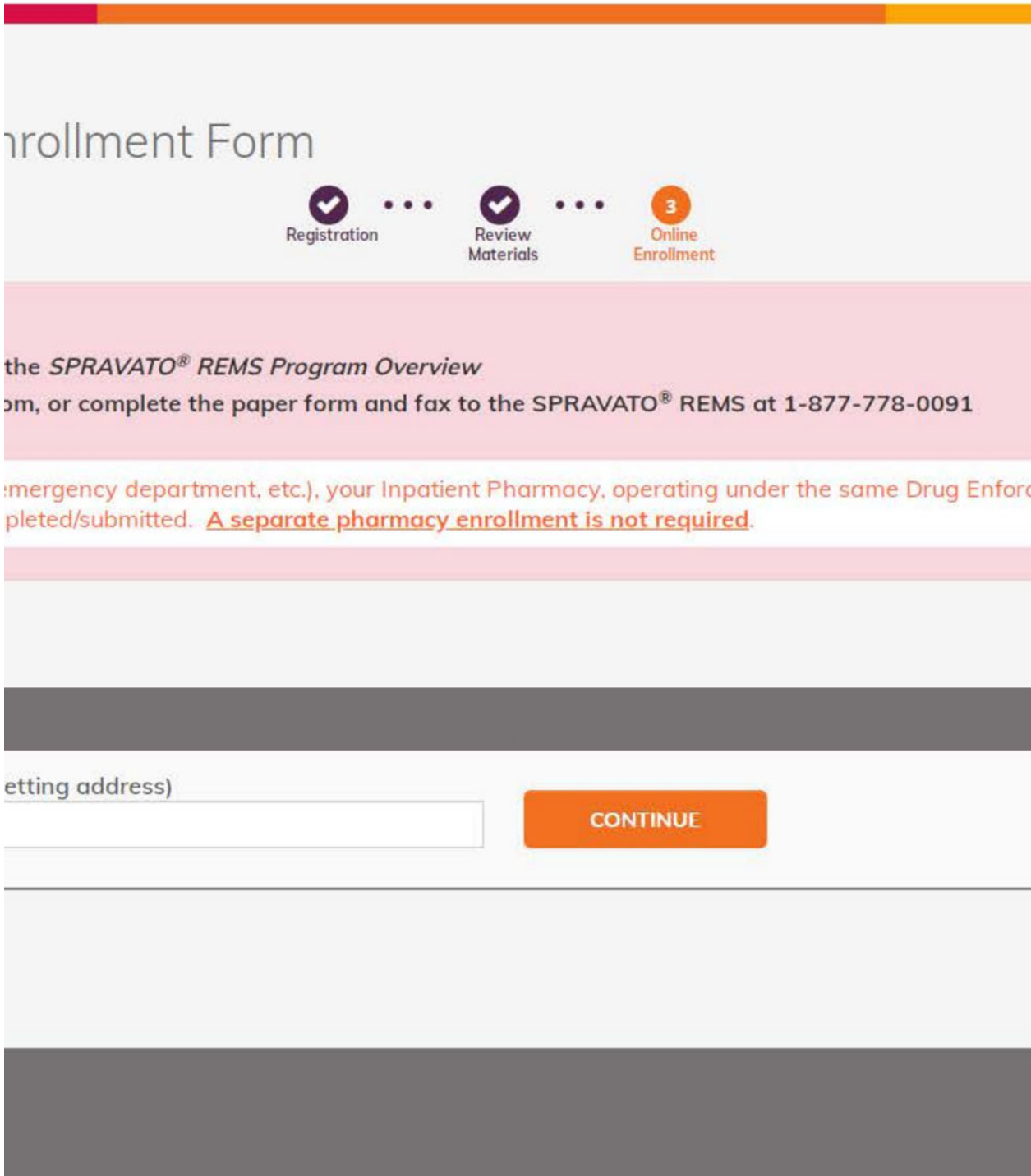
nrollment Form
Registration
Review Materials
3
Online Enrollment
the SPRAVATO® REMS Program Overview
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mergency department, etc.), your Inpatient Pharmacy, operating under the same Drug Enforc
pleted/submitted. A separate pharmacy enrollment is not required.
etting address)
CONTINUE

Spravato® (esketamine) C-III
nasal spray

SPRAVATO® REMS
Inpatient Healthcare Setting Enrollment Form

Registration • • • Review Materials • • •

Instructions

1. Review the SPRAVATO® *Prescribing Information* and the *SPRAVATO® REMS Program Overview*
2. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVA

As an Inpatient Healthcare Setting (with inpatient units, emergency department, etc.), your Inpatient Pharmacy, o location, will be considered certified once this form is completed/submitted. A separate pharmacy enrollment is n

**Indicates Required Field*

Healthcare Setting Information

*DEA License Number (associated with the Healthcare Setting address)
12345

CO

Name of DEA License Holder (if different from Healthcare Setting Name)

*DEA License Expiration Date (MM/DD/YYYY)
99/99/9999

*Healthcare Setting Name
ABC HealthCare

*Healthcare Setting Address 1
123 Main Street

Address

*City
Blue Bell

*State
PA

*Healthcare Setting Telephone Number
555 555-1212

Healthca

*Healthcare Setting Type (select all that apply)

- ☐ Hospital-Emergency Department
- ☐ Hospital-Inpatient
- ☐ Mental Health Facility
- ☐ Other

Spravato® (esketamine) C III
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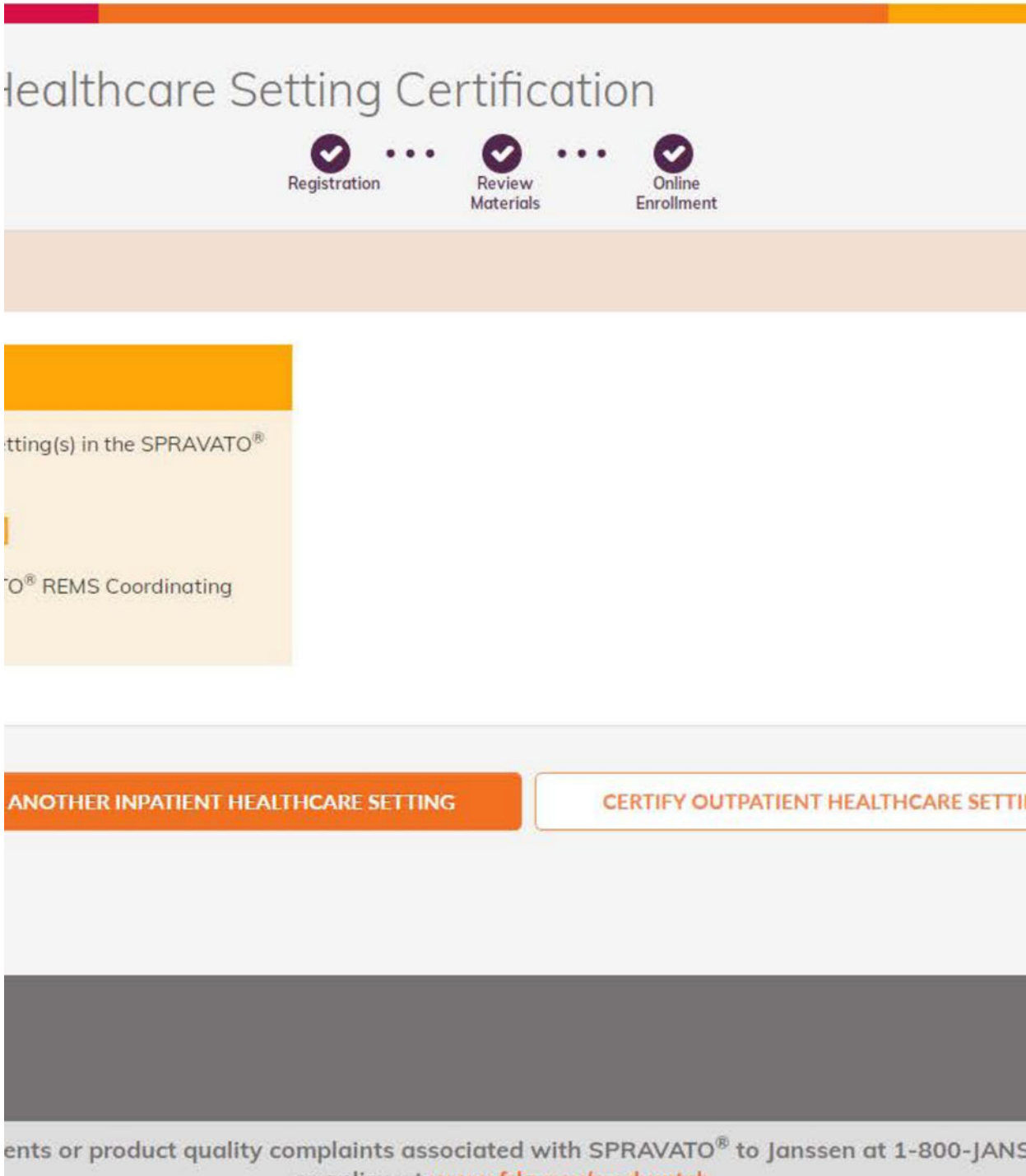
Healthcare Setting Certification
Registration
Review Materials
Online Enrollment
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TO® REMS Coordinating
ANOTHER INPATIENT HEALTHCARE SETTING
CERTIFY OUTPATIENT HEALTHCARE SETTI
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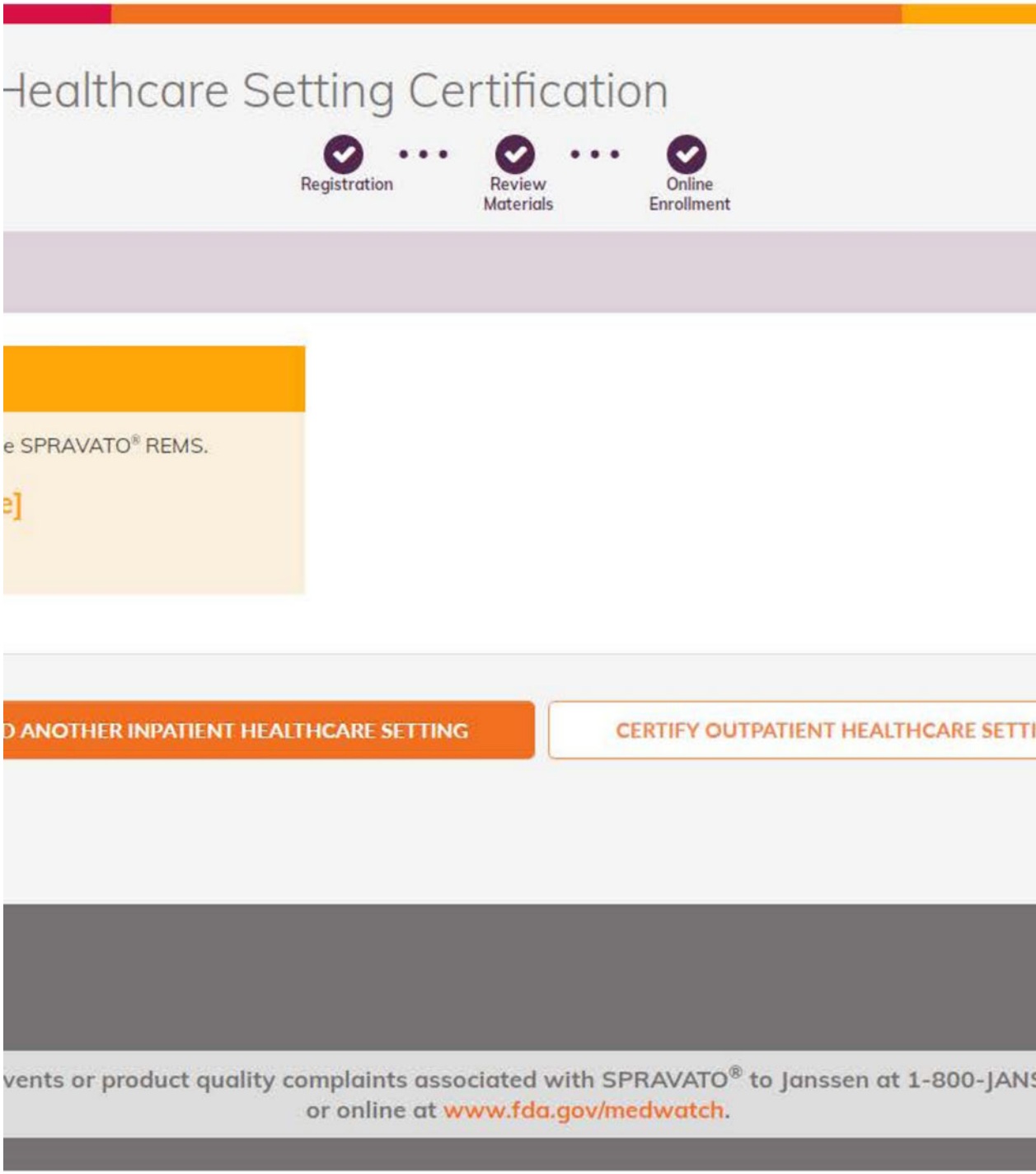
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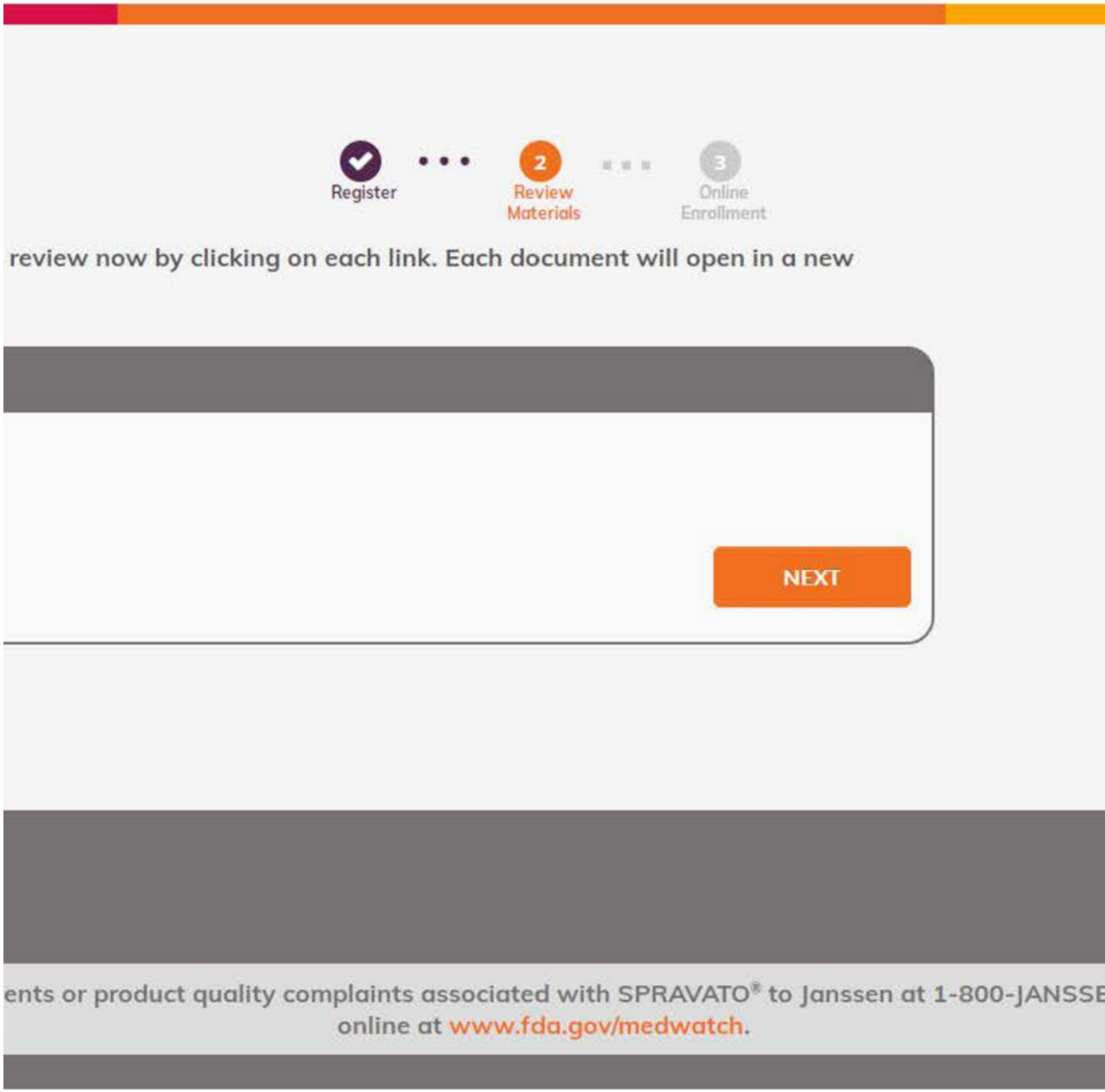
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NEXT
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online at www.fda.gov/medwatch.

Spravato® (esketamine) C III nasal spray

SPRAVATO® REMS
Outpatient Healthcare Setting Enrollment Form

Registration • • • Review Materials • • • 3 Online Enrollment

Instructions

1. Review the SPRAVATO® *Prescribing Information* and the *SPRAVATO® REMS Program Overview*
2. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091

This form is intended only for Outpatient Medical Offices and Clinics.
Emergency departments within hospitals are certified through the Inpatient Healthcare Setting enrollment.

**Indicates Required Field*

Healthcare Setting Information

*DEA License Number (associated with the Healthcare Setting address)

CONTINUE

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com

Spravato® (esketamine) CIII nasal spray

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99/99/9999

*Healthcare Setting Name
ABC HealthCare

*Healthcare Setting Address 1
123 Main Street

Address Li

*City
Blue Bell

*State
PA

*Healthcare Setting Telephone Number
555 555-1212

Healthcare

*Healthcare Setting Type (select all that apply)

- ☐ Mental Health Facility
- ☐ Outpatient Clinic
- ☐ Independent Practice
- ☐ Group Practice
- ☐ Other

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Spravato® (esketamine) C-III nasal spray

SPRAVATO® REMS Outpatient Healthcare Setting Certification

Registration • • • Review Materials • • • Online Enrollment

✔ Complete

Outpatient Healthcare Setting

The Outpatient Healthcare Setting is now certified in the SPRAVATO® REMS.

[Outpatient Healthcare Setting #1 Name]

Please check your email for additional requirements.

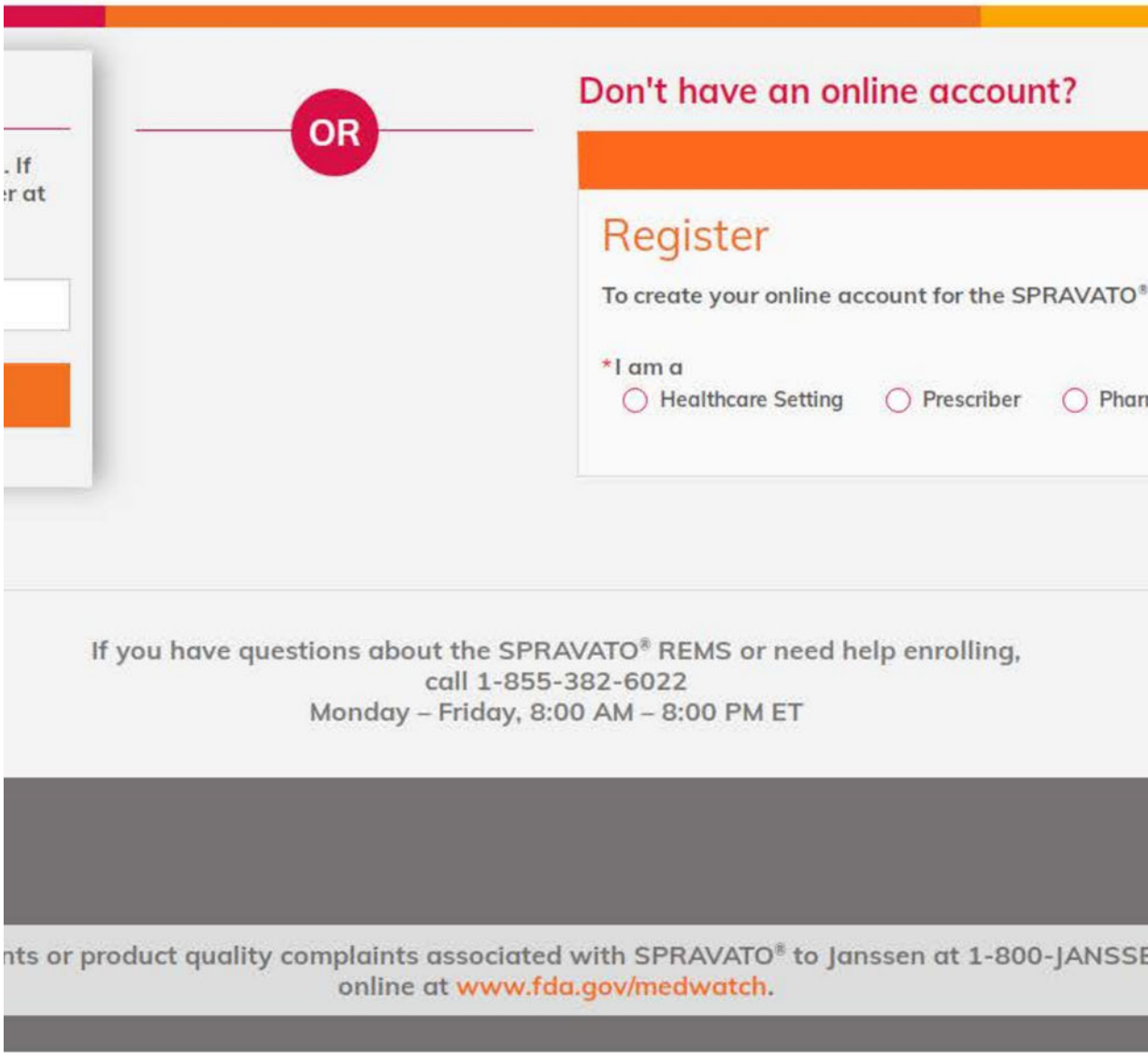
Pending

Outpatient Healthcare Setting

The certification of the following Outpatient Healthcare Setting(s) in the SPRAVATO® REMS is pending.

[Outpatient Healthcare Setting #2 Name]

If you have any questions, please contact the SPRAVATO® REMS Coordinating Center at 1-855-382-6022.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To create your online account for the SPRAVATO®
*I am a
Healthcare Setting
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call 1-855-382-6022
Monday – Friday, 8:00 AM – 8:00 PM ET
nts or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSSE
online at www.fda.gov/medwatch.

Spravato® (esketamine) C III nasal spray

Login

Your username was supplied to you via email when you registered. If you need assistance, please contact the REMS Coordinating Center at 1-855-382-6022.

User Name

Forgot Username

LOGIN

OR

Don't have an online account?

Register

To create your online account for the SPRAVATO

*I am a

Healthcare Setting Prescriber Pha

Pharmacy Authorized Represen

*First Name

*Last Name

*Title

*Telephone Number

*Fax Number

*Email Address

Spravato® (esketamine) C III nasal spray

Account Submitted Successfully

Thank you for submitting your information to create your web account for the SPRAVATO® REMS.

A confirmation of this submission has been sent to the email address provided. You can expect to receive 2 emails, one contains your username and the second contains yo temporary password. Please login with the username provided. You will then be prompted to update your password.

If you do not receive the emails within the next few hours, or would like to update your enrollment information at any time, please contact the SPRAVATO® REMS at 1-855- 6022.

LOGIN

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com

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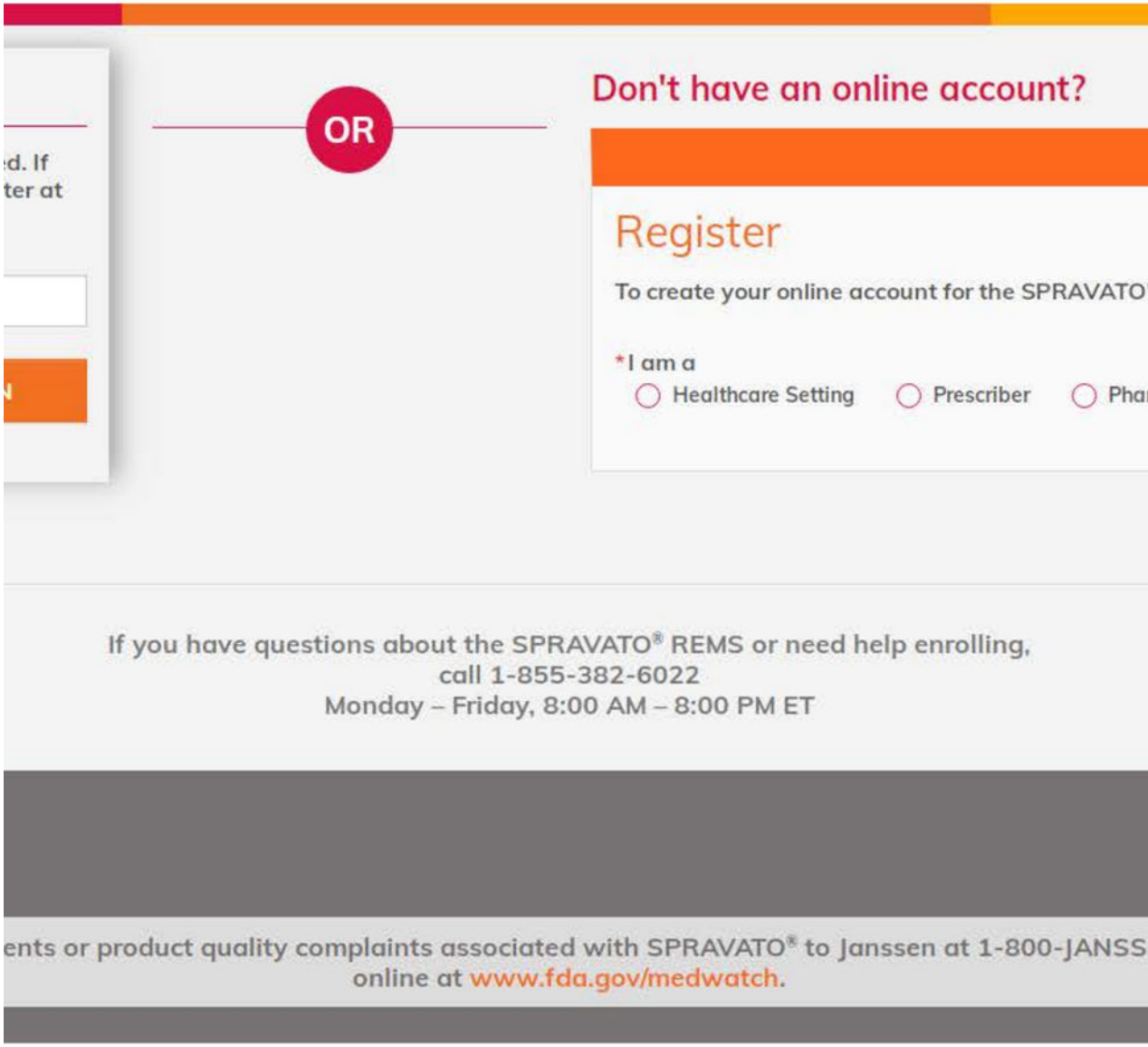
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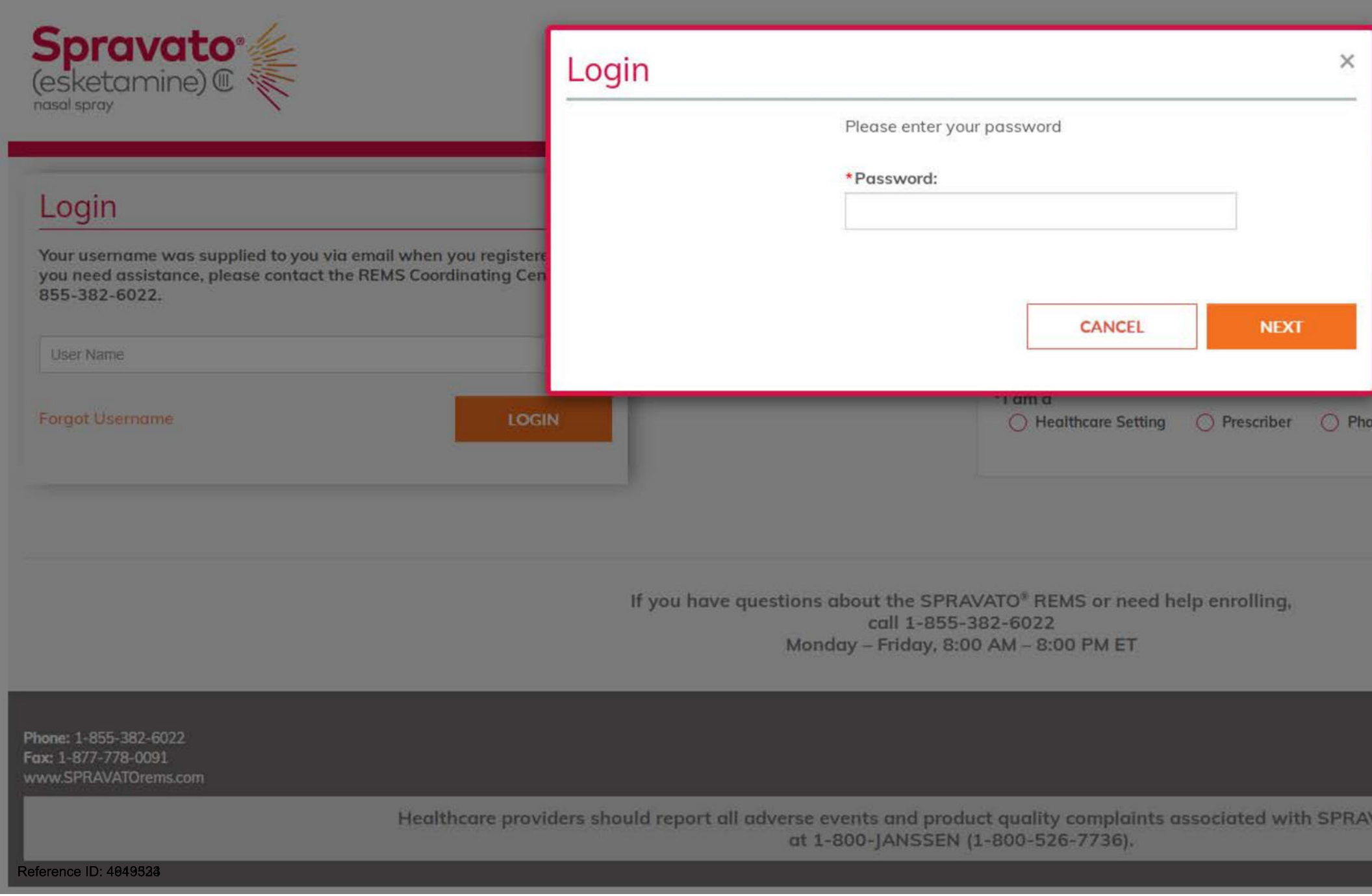
Spravato®
(esketamine) C-III
nasal spray
Login
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User Name
Forgot Username
LOGIN
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Please enter your password
*Password:
CANCEL
NEXT
Healthcare Setting
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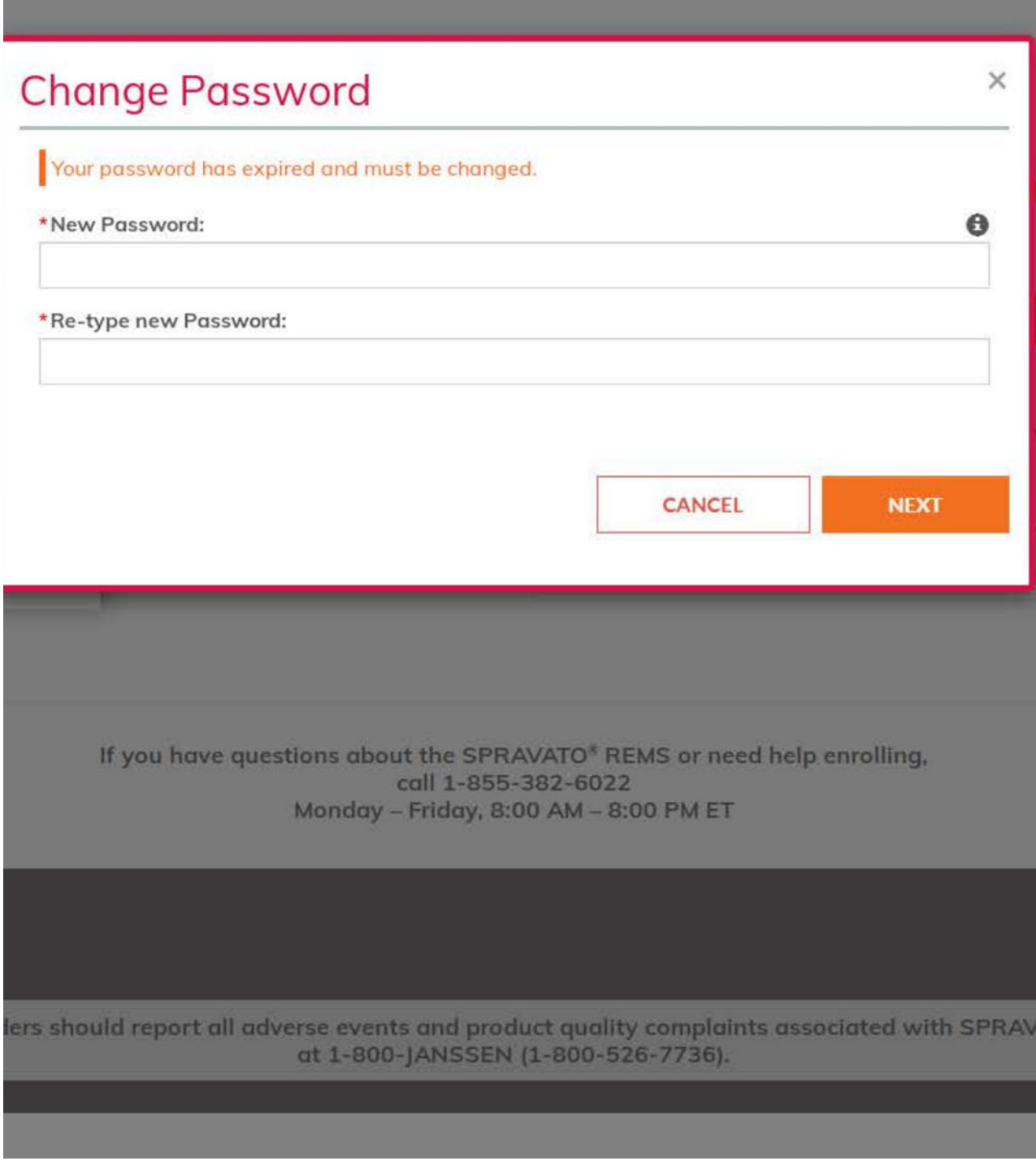
Change Password
Your password has expired and must be changed.
*New Password:
*Re-type new Password:
CANCEL
NEXT
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Spravato® (esketamine) C III nasal spray

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User Name

Forgot Username

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Fax: 1-877-778-0091
www.SPRAVATOrems.com

Healthcare provi

Update Profile









*Security Caption:

*Security Question | *Answer

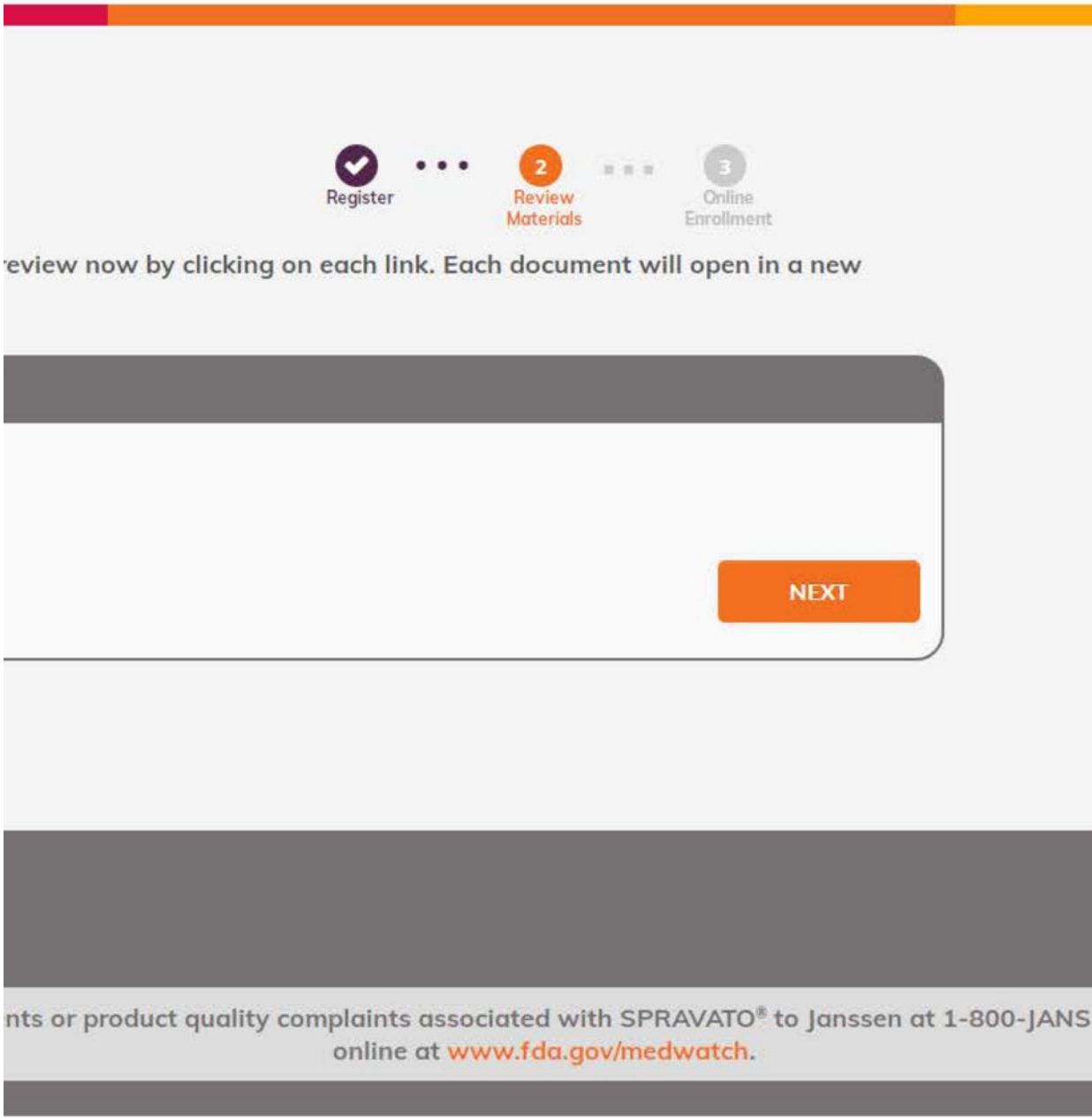
-- Please Select -- | Answer

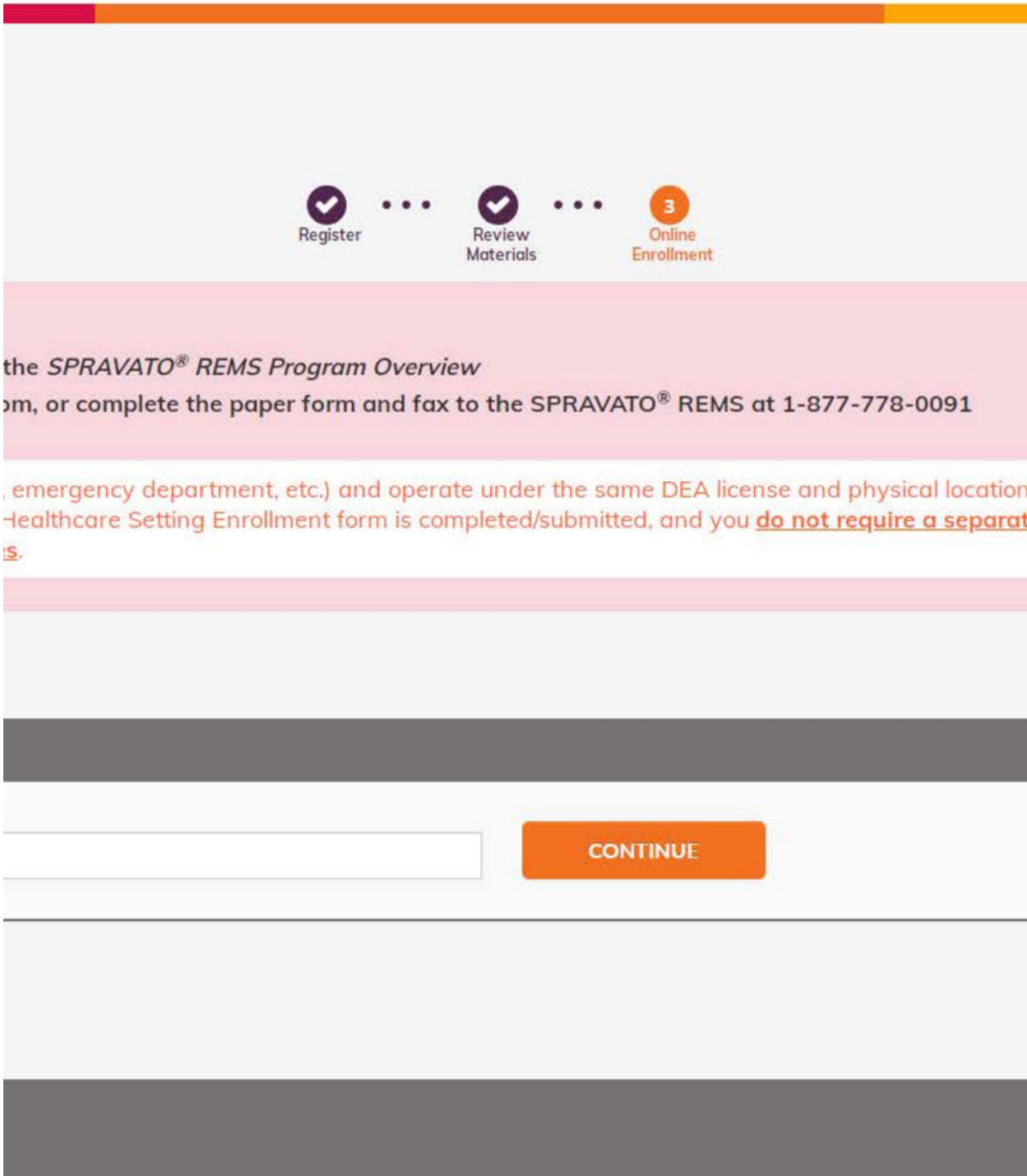
-- Please Select -- | Answer

-- Please Select -- | Answer

CANCEL NEXT

Reference ID: 4049523


Register
2
Review Materials
3
Online Enrollment
eview now by clicking on each link. Each document will open in a new
NEXT
nts or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANS
online at www.fda.gov/medwatch.


Register
Review Materials
3
Online Enrollment
the SPRAVATO® REMS Program Overview
om, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091
, emergency department, etc.) and operate under the same DEA license and physical location
Healthcare Setting Enrollment form is completed/submitted, and you do not require a separat
s.
CONTINUE

Spravato® (esketamine) C III nasal spray

SPRAVATO® REMS Pharmacy Enrollment Form

Register • • • Review Materials • • •

Instructions

1. Review the *SPRAVATO® Prescribing Information* and the *SPRAVATO® REMS Program Overview*
2. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVAT

If you are an Inpatient Pharmacy (support inpatient units, emergency department, etc.) and operate under the sam pharmacy will be considered certified once the Inpatient Healthcare Setting Enrollment form is completed/submitte only for pharmacies that dispense to outpatient facilities.

* *Indicates Required Field*

Pharmacy Information

*DEA License Number (On file with distributor account)

2345

CON

*DEA Expiration Date (MM/DD/YYYY):

99/99/9999

*Name of Pharmacy

ABC Pharmacy

*Pharmacy Address 1

123 Main Street

Address L

*City

Blue Bell

*State

PA

*ZIP

99999

*Pharmacy Type (select all that apply)

☐ Community/Retail ☐ Specialty ☐ Other

Your pharmacy information will be shared with Janssen's patient support and distribution partners, to allow yo

Pharmacy Shipping Address, if different from above

Spravato® (esketamine) CIII nasal spray

SPRAVATO® REMS Pharmacy Enrollment Form

Register • • • Review Materials • • •

Instructions

1. Review the *SPRAVATO® Prescribing Information* and the *SPRAVATO® REMS Program Overview*
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2345

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*DEA Expiration Date (MM/DD/YYYY):

99/99/9999

*Name of Pharmacy

ABC Pharmacy

*Pharmacy Address 1

123 Main Street

Address Li

*City

Blue Bell

*State

PA

*ZIP

99999

*Pharmacy Type (select all that apply)

☐ Community/Retail ☐ Specialty ☑ Other

*Other Pharmacy Type

Other

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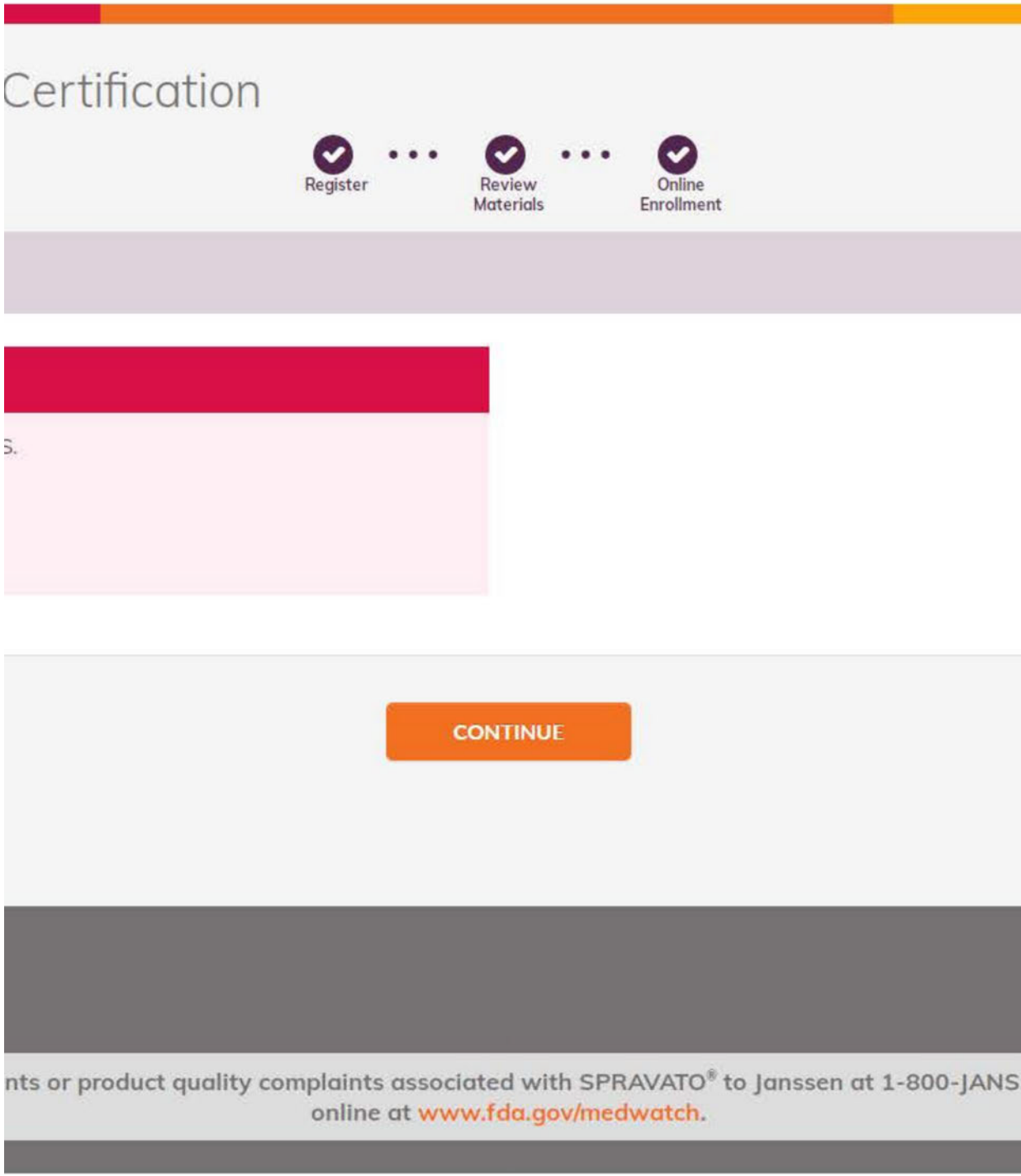
Certification
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Review Materials
Online Enrollment
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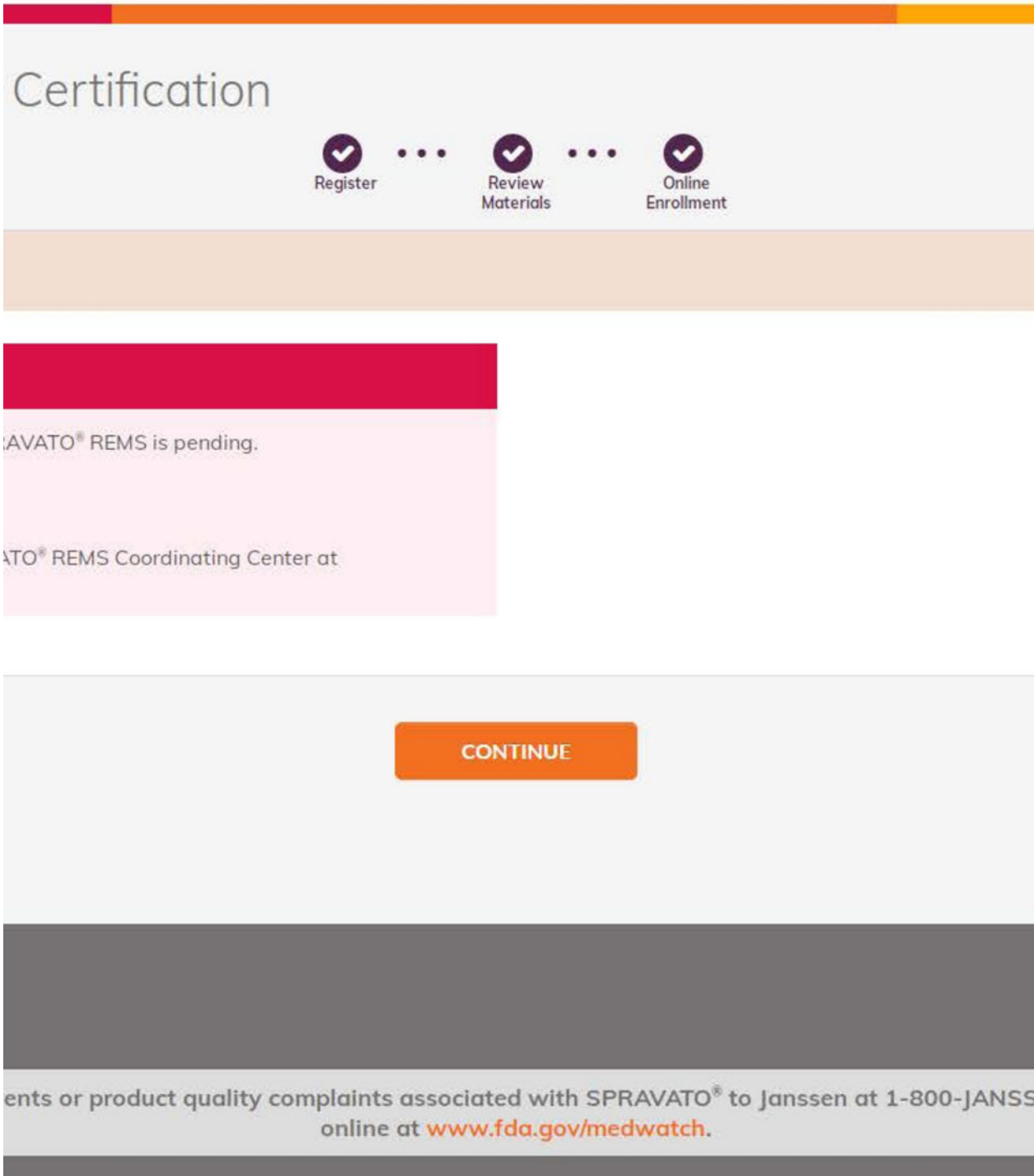
online at www.fda.gov/medwatch.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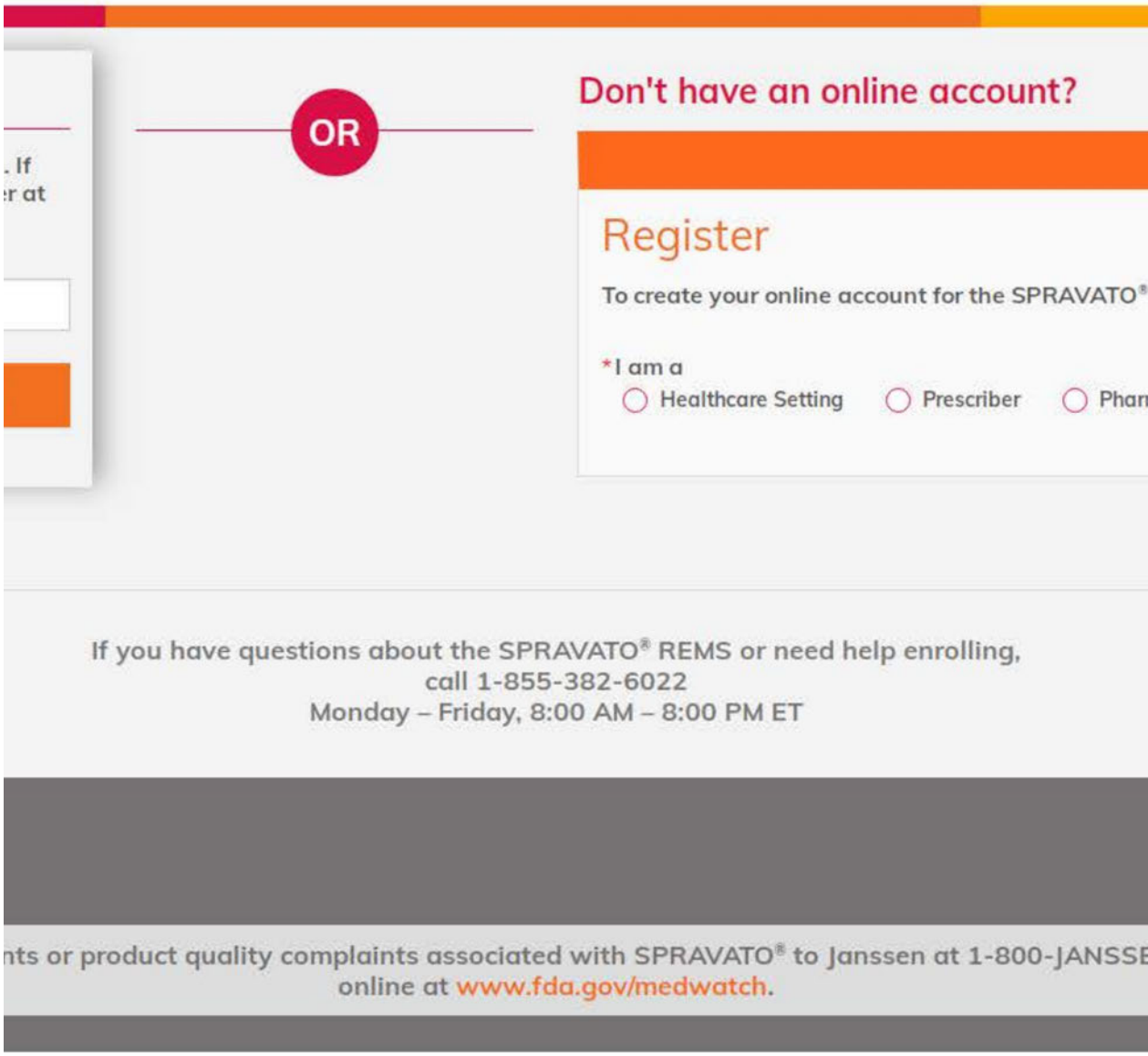
online at www.fda.gov/medwatch.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If you have questions about the SPRAVATO® REMS or need help enrolling,
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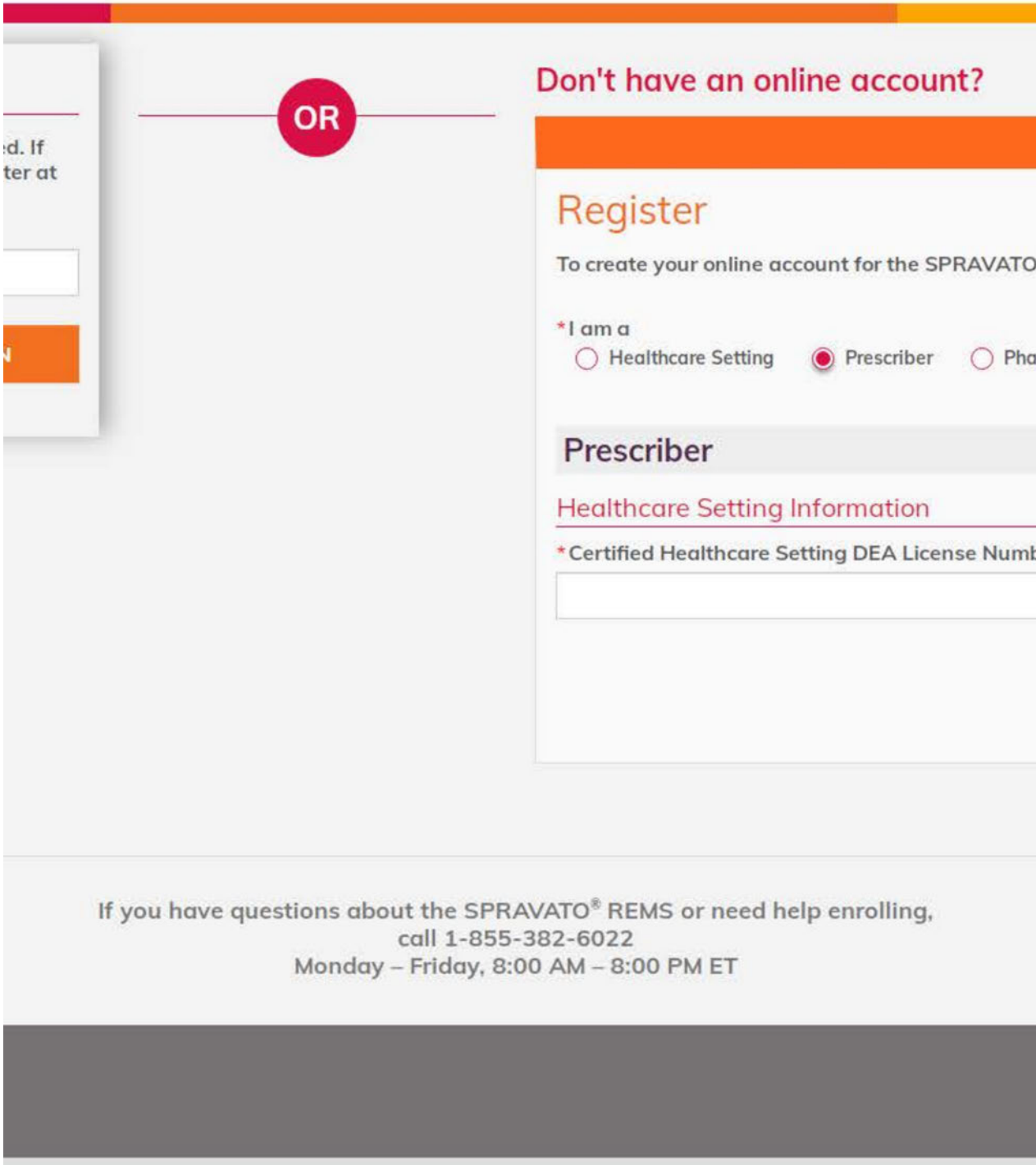
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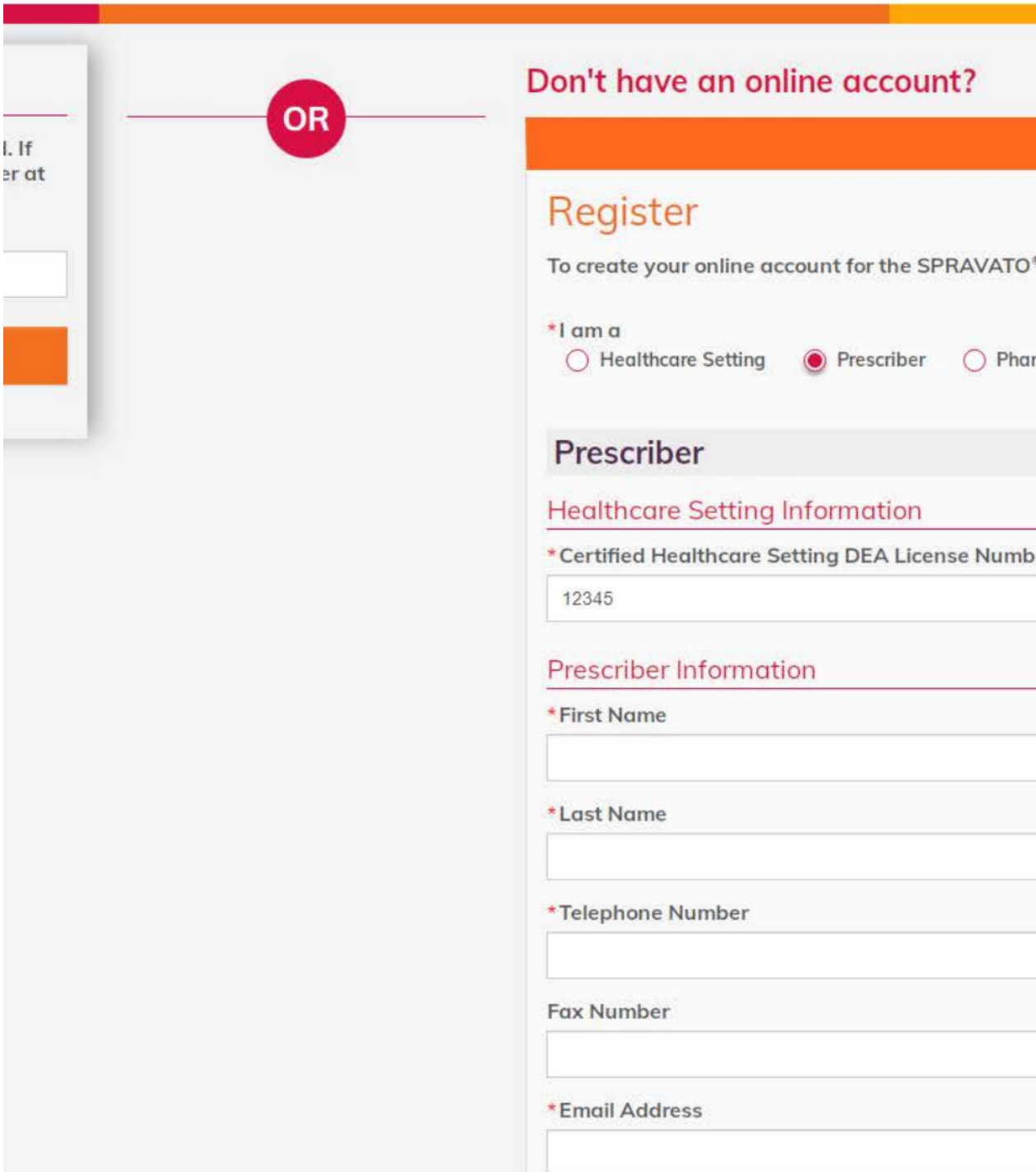
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*Certified Healthcare Setting DEA License Numb
12345
Prescriber Information
*First Name
*Last Name
*Telephone Number
Fax Number
*Email Address

Spravato® (esketamine) C-III nasal spray

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User Name

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LOGIN

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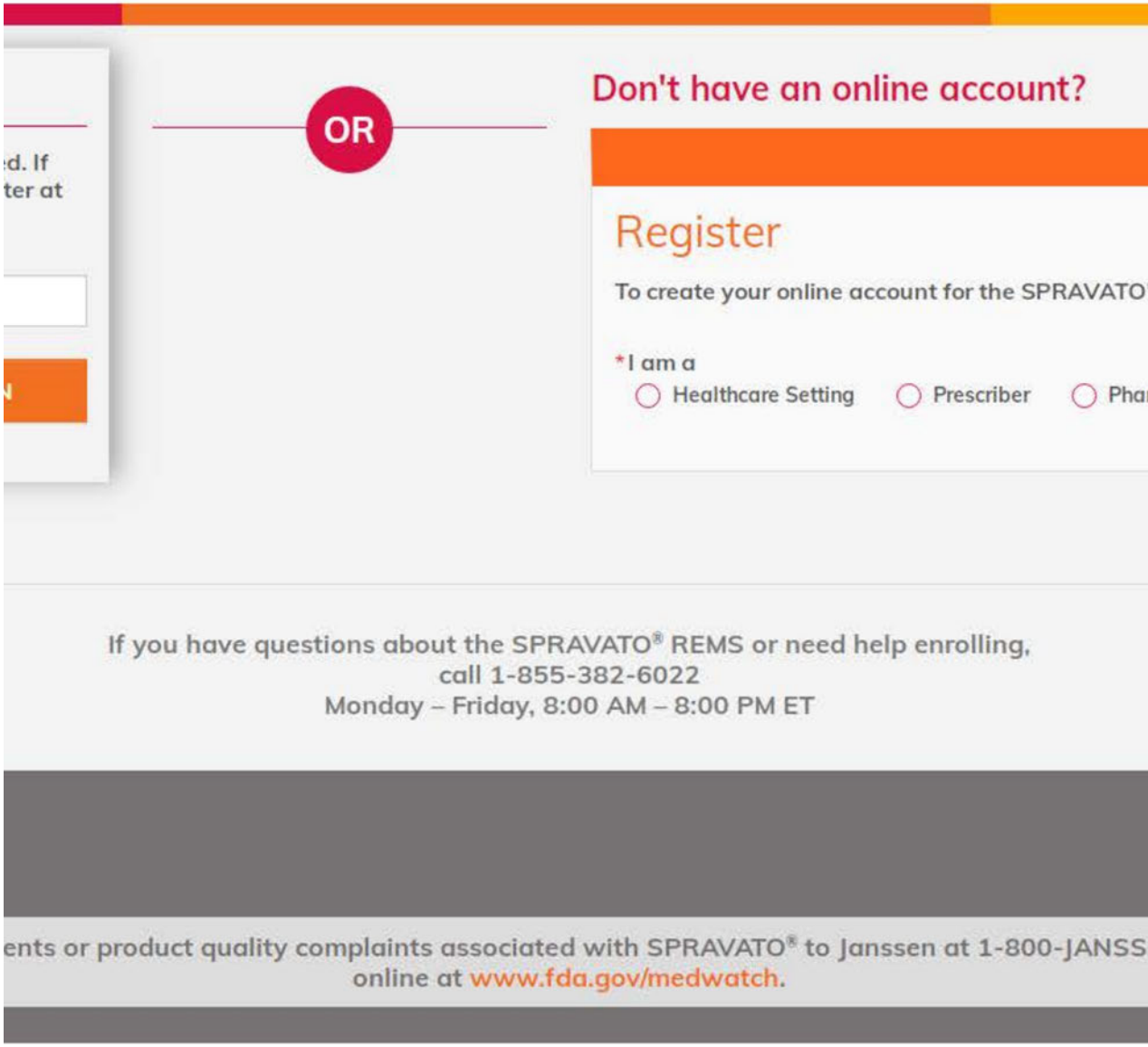
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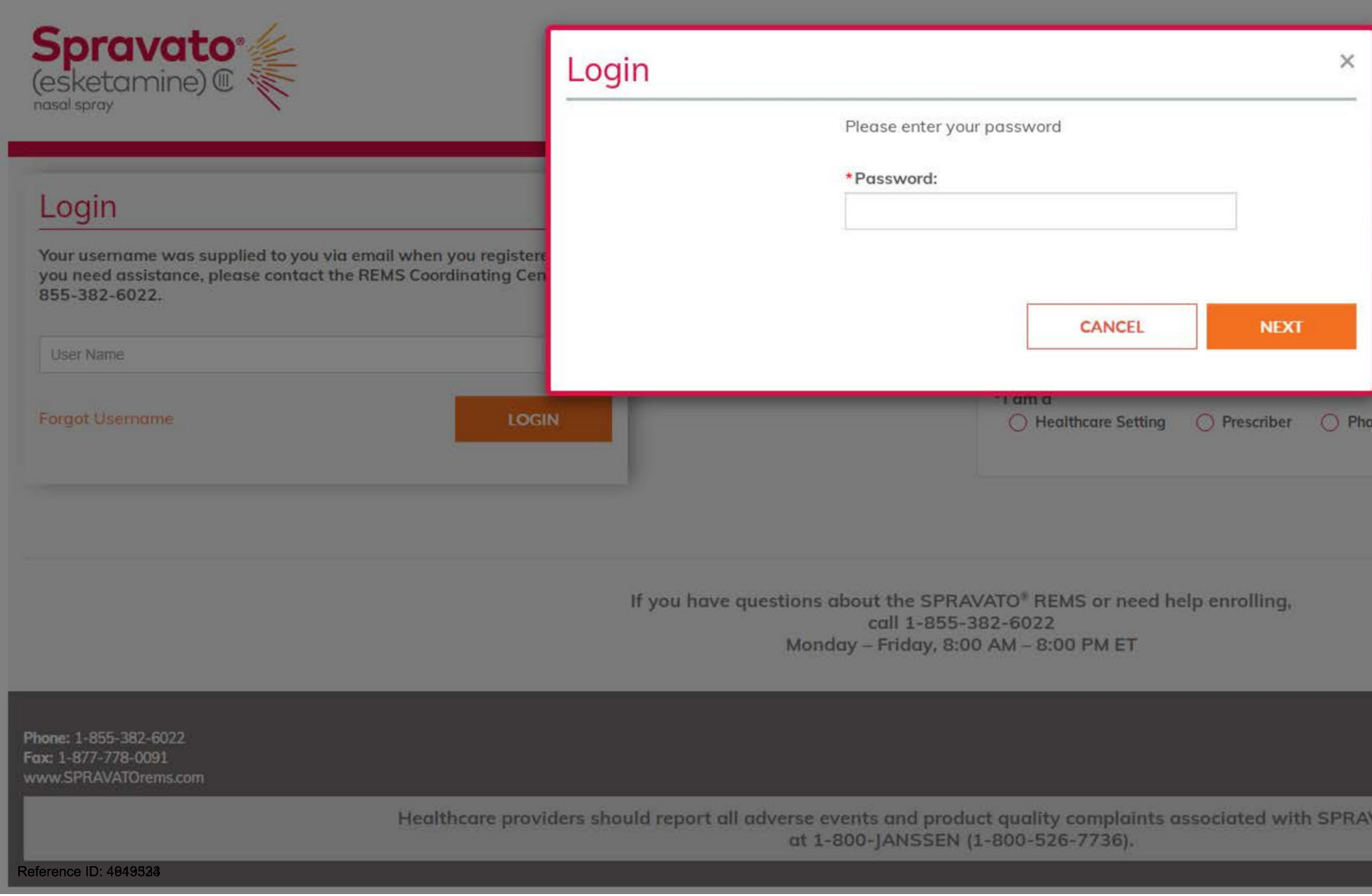
Spravato®
(esketamine) C-III
nasal spray
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User Name
Forgot Username
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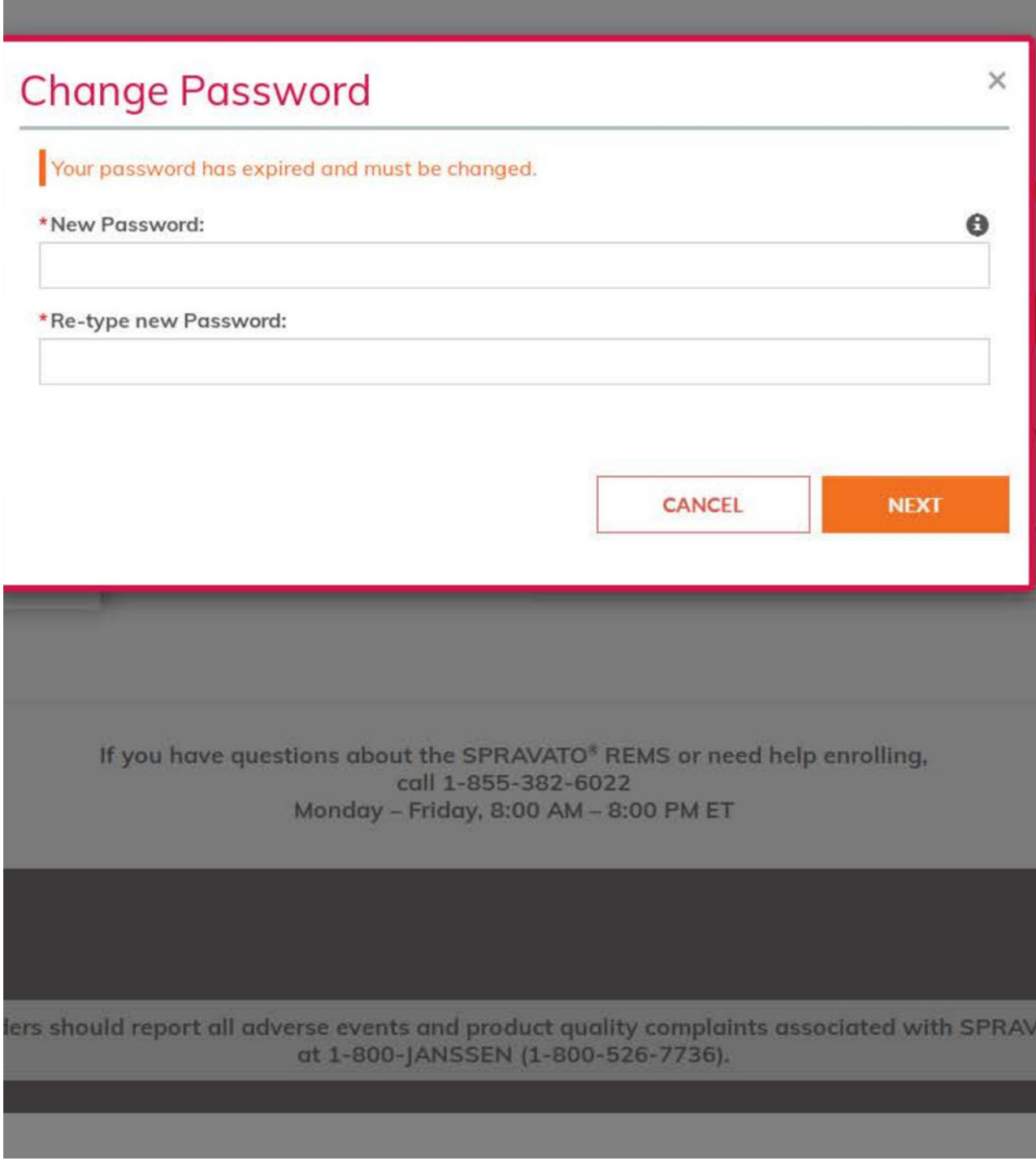
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www.SPRAVATOrems.com

Healthcare provi

Update Profile









*Security Caption:

*Security Question | *Answer

-- Please Select -- | Answer

-- Please Select -- | Answer

-- Please Select -- | Answer

CANCEL NEXT

Reference ID: 4049523

Spravato® (esketamine) C III
nasal spray

MY PATIENTS | CERTIFIED PHARMACIES | DELEGATE MANAGEMENT

My Patients

Below is a list of your patients.

Enroll a Patient ▸

Patient Listing

- Download the list to spreadsheet format by clicking the Excel icon just above the column headers.
- Search/Filter the list by entering information in the textbox below any column header.
- Sort the list by clicking on any column header.
- Click on Patient REMS ID to view treatment history.

If you w
cannot

Patient REMS ID	First Name	Last Name	Address	City	State	Zip
111111	Robert	Smith	123 Main Street	Philadelphia	PA	19042
22222	Mary	Connors	3 Broadway	Blue Bell	PA	19042

Spravato® (esketamine) C III
nasal spray

MY PATIENTS | CERTIFIED PHARMACIES | DELEGATE MANAGEMENT

SPRAVATO® REMS
Patient Monitoring Form - Outpatient Use Only

Instructions

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments.

1. Complete all required fields on this form after **every** treatment session for **all outpatients** enrolled in the SPRAVATO® REMS.
2. Submit completed patient monitoring forms within **7 days**, online at www.SPRAVATOrems.com or by fax (1-877-778-0091).

**Indicates Required Field*

Patient Information

First Name: Peggy
Middle Initial:
Birthdate (MM/DD/YYYY): 1/1/2000
Sex: Female

Concomitant Medications

Is the patient currently taking any of the following medication(s) that may cause sedation or blood pressure cha

*Benzodiazepines
○ Yes ○ No

*Non-benzodiazepine sedative hypnotics
○ Yes ○ No

*Psychostimulants
○ Yes ○ No

*Monoamine oxidase inhibitors (MAOIs)
○ Yes ○ No

Healthcare Provider Conducting Patient Monitoring

*First Name
John

*Last Nam
Smith

*Telephone
555 555-1212

*Email
jsmith@abc

Spravato® (esketamine) C III
nasal spray

MY PATIENTS | CERTIFIED PHARMACIES | DELEGATE MANAGEMENT

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*Monoamine oxidase inhibitors (MAOIs)
○ Yes ○ No

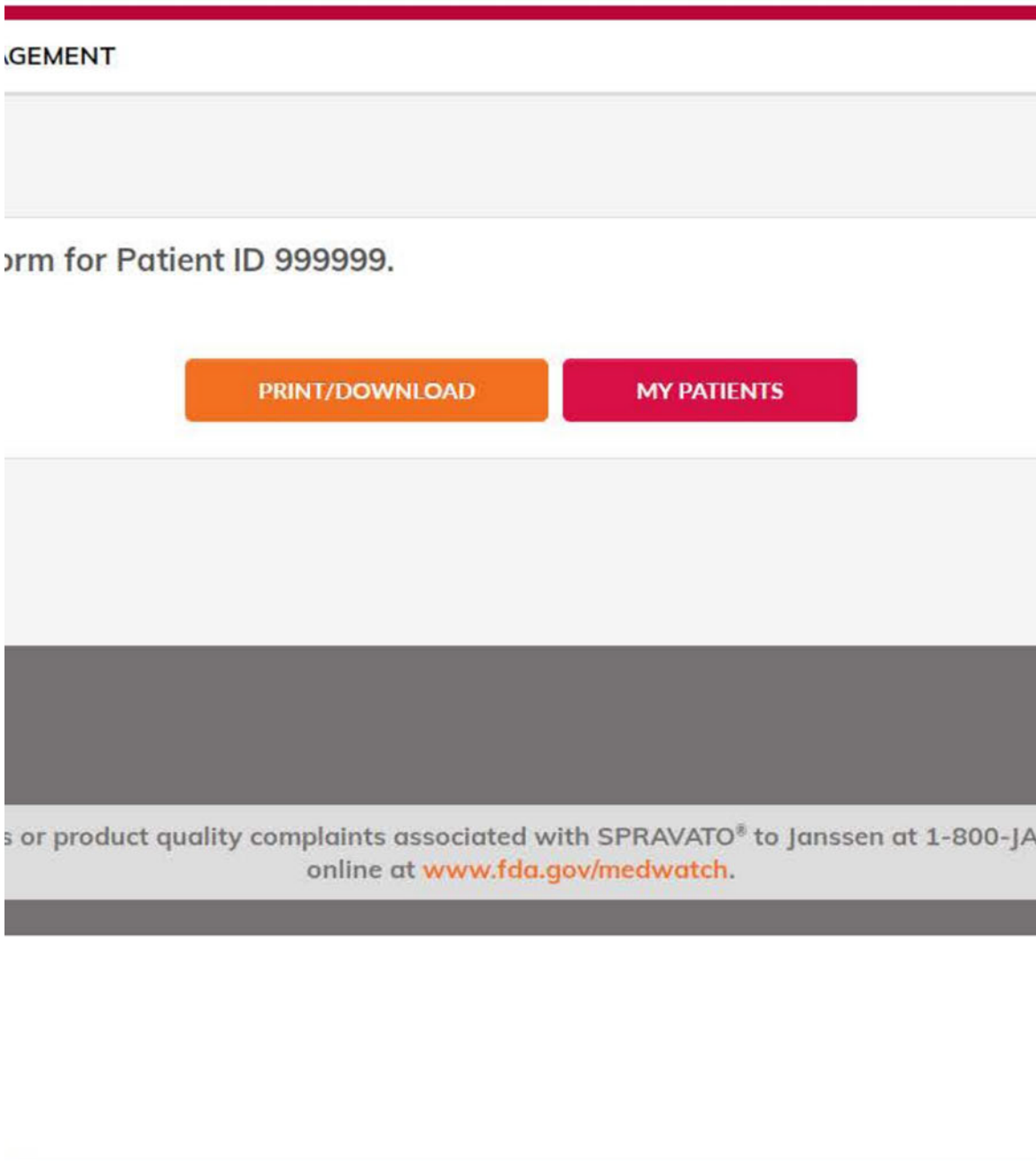
Healthcare Provider Conducting Patient Monitoring

*First Name
John

*Last Nam
Smith

*Telephone
555-555-1212

*Email
jsmith@abc


GEMENT
rm for Patient ID 999999.
PRINT/DOWNLOAD
MY PATIENTS
s or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JA
online at www.fda.gov/medwatch.

Spravato® (esketamine) nasal spray

SPRAVATO® REMS

Patient Monitoring Form - Outpatient Use Only

For Healthcare Setting Use Place Patient Label or Barcode Here

INSTRUCTIONS:

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2. Submit completed patient monitoring forms within **7 days**, online at www.SPRAVATOrems.com or by fax (1-877-778-0091).

** Indicates Required Field*

Patient Information (PRINT)

First Name*:	MI:	Last Name*:	Birthdate* (MM/DD/YYYY):	Sex*: ☐ Male ☐ Female ☐ Other

Concomitant Medication

Is the patient currently taking any of the following medication(s) that may cause sedation or blood pressure changes?

- Benzodiazepines* ☐ Yes ☐ No
- Non-benzodiazepine sedative hypnotics* ☐ Yes ☐ No
- Psychostimulants* ☐ Yes ☐ No
- Monoamine oxidase inhibitors (MAOIs)* ☐ Yes ☐ No

Healthcare Provider Conducting Patient Monitoring (PRINT)

First Name*:	Last Name*:
Telephone*:	Email*:

Healthcare Setting Information (PRINT)

Healthcare Setting Name*:		
Healthcare Setting Address 1*:	Healthcare Setting Address 2:	
City*:	State*:	ZIP*:

Patient Treatment Session Information (Administration and Monitoring)

Treatment Date*	Date (MM/DD/YYYY): _____	
Dose Administered*	☐ 56 mg ☐ 84 mg ☐ Other: _____	**Lot Number***: _____
Treatment Duration*	Total time _____ minutes (from 1st device administration to completion of monitoring) Patient must be monitored for at least 2 hours	
REMS Evaluation Question*	*If patient was not for 2-hour minimum monitoring requirement, when would this patient have been ready to leave / no longer require monitoring?* _____ *minutes from start of administration*	
Monitoring of Vital Signs*	Vital signs were in acceptable range **prior** to: • administration? ☐ Yes ☐ No • treatment session completion? ☐ Yes ☐ No	
Monitoring of Blood Pressure*	**Prior to administration** _____/_____ mmHg	**40 mins post-administration** _____/_____ mmHg / **Prior to treatment session completion** _____/_____ mmHg

Did the patient experience Sedation and/or Dissociation

Sedation*: ☐ Yes ☐ No	**Dissociation***: ☐ Yes ☐ No
Onset of symptoms from start of administration* ☐ 1-29 mins ☐ 30-59 mins ☐ 60-89 mins ☐ 90-120 mins ☐ >120 mins	**Onset of symptoms** from start of administration* ☐ 1-29 mins ☐ 30-59 mins ☐ 60-89 mins ☐ 90-120 mins ☐ >120 mins
Resolution of symptoms within 2 hours?* ☐ Yes ☐ No Specify total time to resolution*: _____minutes	**Resolution of symptoms** within 2 hours?* ☐ Yes ☐ No Specify total time to resolution*: _____minutes
Medication(s) given for sedation?* ☐ Yes ☐ No •If YES, name and dose of medication(s): _____	**Medication(s) given for dissociation?*** ☐ Yes ☐ No •If YES, name and dose of medication(s): _____

Spravato® (esketamine) C III
nasal spray

MY PATIENTS | CERTIFIED PHARMACIES | DELEGATE MANAGEMENT

SPRAVATO® REMS
Patient Enrollment Form - Outpatient Use Only

Instructions

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1. **Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVA**

**Indicates required field*

Healthcare Setting Information

Change Healthcare Setting ▸

Healthcare Setting DEA License Number (associated with the Healthcare Setting address): 12345
Healthcare Setting Name:
Address 1: 100 Main Street
City: Malvern
Phone: 555 555-1212
Address 2
State: PA
Fax: 555 5

Prescriber Information

*First Name: Marc
*Last Nam: Jones

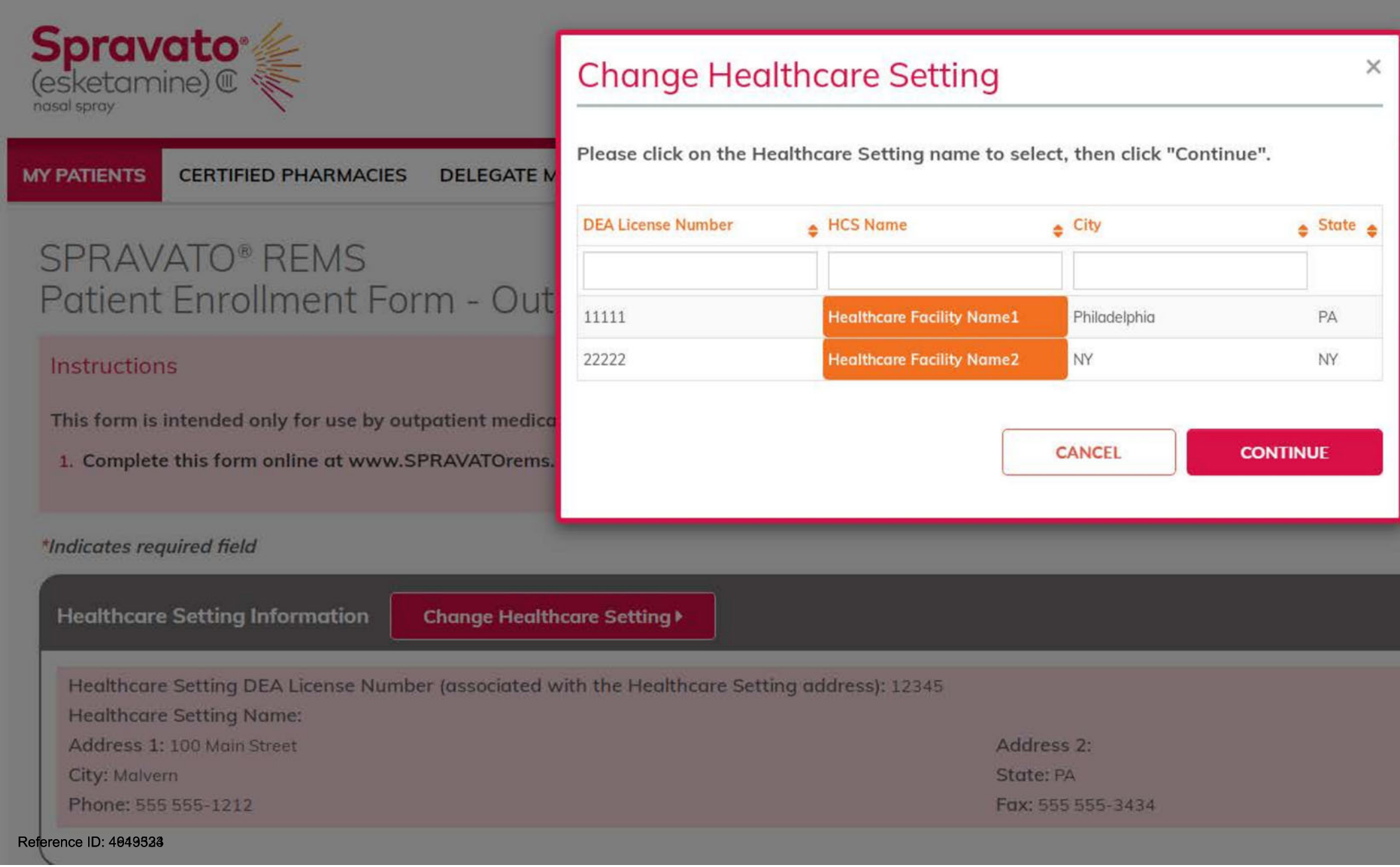
*Credentials: (●) Physician ( ) Physician Assistant ( ) Nurse ( ) Pharmacist ( ) Other
*Specialty: ( ) Psychi

*Prescriber DEA License Number: 12345
*Email: mjones@ab

*Phone: 555 555-1212
Fax: 555 555-34

Referring Healthcare Provider - if different from Prescriber

☐ Referring Healthcare Provider- Same as Prescriber



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Indicates required field

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Fax: 555 5

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*Credentials
(●) Physician ( ) Physician Assistant ( ) Nurse ( ) Pharmacist ( ) Other

*Specialty
( ) Psychi

*Prescriber DEA License Number: 12345
*Email: mjones@ab

*Phone: 555 555-1212
Fax: 555 555-343

Referring Healthcare Provider - if different from Prescriber

☑ Referring Healthcare Provider- Same as Prescriber

Welcome — Agree to Terms — Sign — Done

1 — 2 — 3 — 4

A new document from SPRAVATO® REMS is available for you to sign.

You will be given the opportunity to:

- Preview the document.
- Send feedback or questions to SPRAVATO® REMS.
- Decline signing and send feedback to SPRAVATO® REMS.
- Sign the document electronically using AssureSign.

Continue

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Spravato (esketamine) C
nasal spray

Welcome — Agree to Terms — Sign — Done

Review the terms and conditions below and check the checkbox indicating your agreement to receive and sign this document electronically. Click **Start Signing** when you are ready to sign.

By checking the box below, I agree that the electronic digitized signatures I apply on the following document are representations of my signature and are legally valid and binding as if I had signed the document with ink on paper in accordance with the Uniform Electronic Transactions Act (UETA) and the Electronic Signatures in Global and National Commerce Act (E-SIGN) of 2000.

AssureSign complies with requirements and standards of the Electronic Signatures In Global and National Commerce Act (E-SIGN Act) effective October 1, 2000, the Uniform Electronic Transaction Act (UETA), and the Government Paperwork Elimination Act (GPEA)

I have read and agree to the terms and conditions

Preview Document

Start Signing

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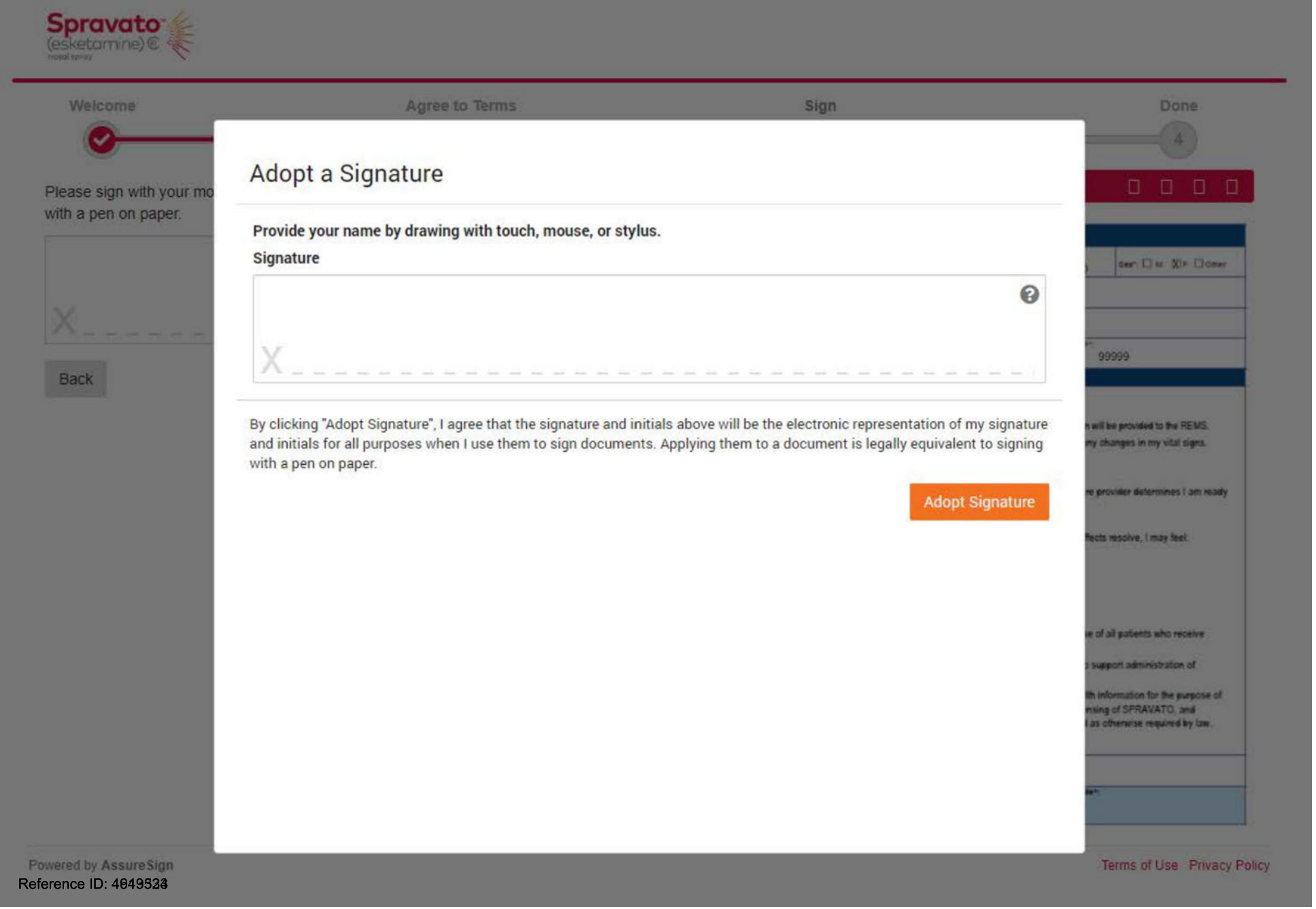
Reference ID: 4849528



Reference ID: 4949523

Spravato® (esketamine) C-IV nasal spray

Welcome ✓ — Agree to Terms ✓ — Sign ● — Done 4

All Information Entered

You have entered all requested information and signatures.

When ready, click Finish to complete this step of the document signing process.

Back | Finish

1 ▾ of 2

(esketamine) C-IV nasal spray

Patient Enrollment Form - Outpatient Use Only

INSTRUCTIONS:

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments

1. Complete this form online at www.SPRAVATOrems.com, or complete the paper form and fax to the SPRAVATO® REMS at 1-877-778-0091

This section is to be completed by the Prescriber

** Indicates required field*

Healthcare Setting Information

Healthcare Setting Name*: Professtional Testing Facility		
Healthcare Setting DEA License Number* (associated with the Healthcare Setting address): 99999		
Address 1*: 999 Broadway	Address 2:	
City*: Philadelphia	State*: PA	ZIP*: 99999
Phone*: 555-555-1212	Fax*: 555-555-3434	

Prescriber Information

First Name*: John	Last Name*: Smith	
Credentials*: [X] Physician [ ] Physician Assistant [ ] Nurse [ ] Pharmacist [ ] Other _____ Specialty*: [X] Psychiatry [ ] Internal Medicine [ ] Family Practice [ ] Other_____		Prescriber DEA License Number*: 444444
Phone*: 555-5557777	Fax: 555-555-8888	Email*: jsmith@xyz.com
Prescriber Signature*:		Date*:

Referring Healthcare Provider – if different from Prescriber

First Name:	Last Name:

Spravato® (esketamine) C
nasal spray

Welcome — Agree to Terms — Sign — Done

1 — 2 — 3 — 4

A new document from SPRAVATO® REMS is available for you to sign.

You will be given the opportunity to:

- Preview the document.
- Send feedback or questions to SPRAVATO® REMS.
- Decline signing and send feedback to SPRAVATO® REMS.
- Sign the document electronically using AssureSign.

UserName: abc@abc.com

Note - Please check your email for the password.

Password*

Continue

Powered by **AssureSign**

Terms of Use Privacy Policy

Reference ID: 4949524

Spravato (esketamine) nasal spray

Welcome | Agree to Terms | Sign | Done

Review the terms and conditions below and check the checkbox indicating your agreement to receive and sign this document electronically. Click **Start Signing** when you are ready to sign.

By checking the box below, I agree that the electronic digitized signatures I apply on the following document are representations of my signature and are legally valid and binding as if I had signed the document with ink on paper in accordance with the Uniform Electronic Transactions Act (UETA) and the Electronic Signatures in Global and National Commerce Act (E-SIGN) of 2000.

AssureSign complies with requirements and standards of the Electronic Signatures In Global and National Commerce Act (E-SIGN Act) effective October 1, 2000, the Uniform Electronic Transaction Act (UETA), and the Government Paperwork Elimination Act (GPEA)

I have read and agree to the terms and conditions

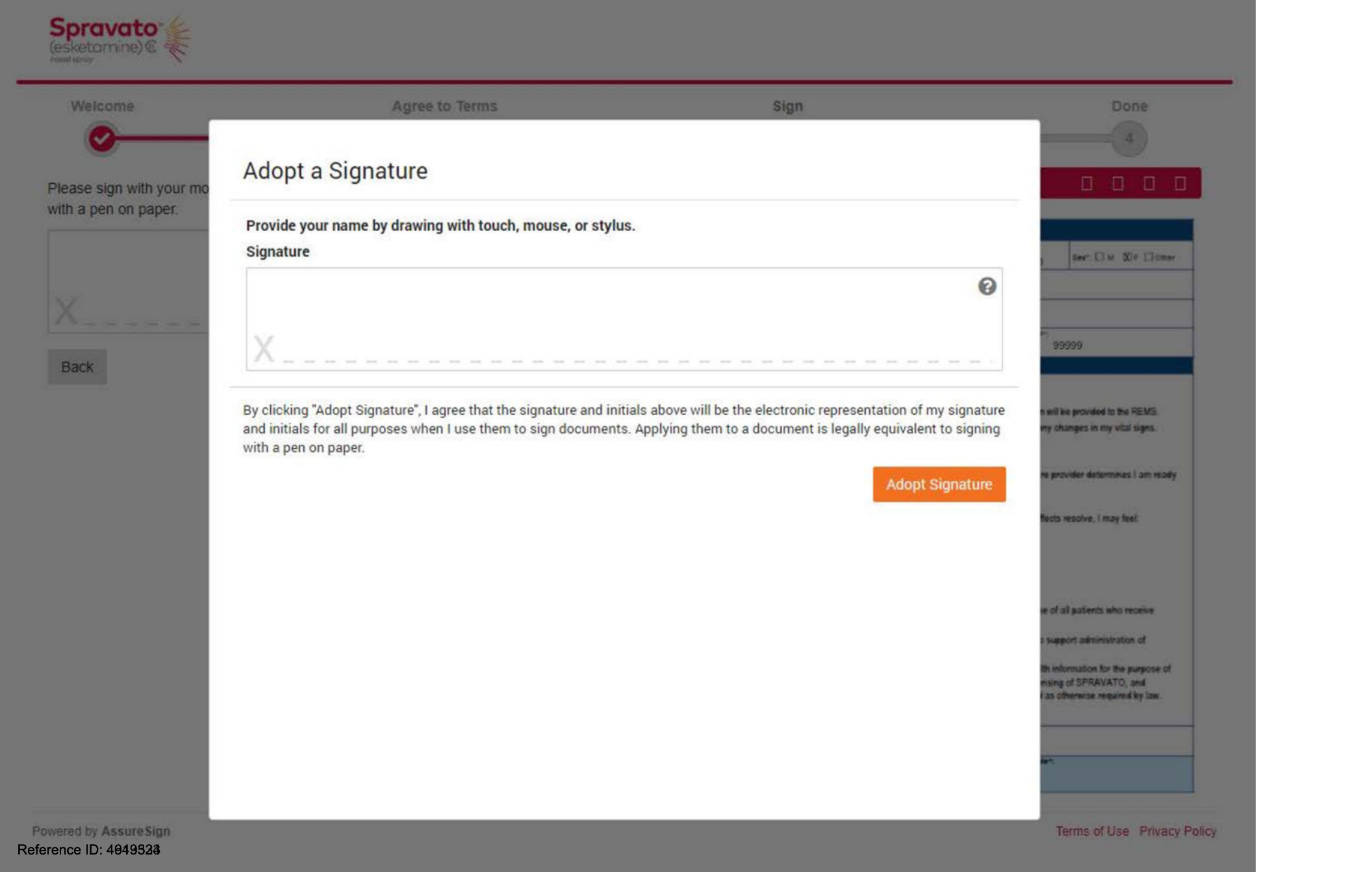
Preview Document

Start Signing

Powered by **AssureSign**

Terms of Use Privacy Policy

Reference ID: 4949523



Spravato® (esketamine) C-IV nasal spray

Welcome — Agree to Terms — Sign — Done (4)

All Information Entered

You have entered all requested information and signatures.

When ready, click Finish to complete this step of the document signing process.

Back | Finish

1 ▾ of 2

Patient Information

First Name*:	MI:	Last Name*:	Birthdate*: (MM/DD/YYYY):	Sex*:
Mary		Smith	1/1/2000	☐ Male ☒ Female ☐ Other

Email*: (Email is required for online enrollment only)	Phone Number*:
abc@abc.com	555-555-1212

Address 1*:	Address 2:
100 Main St	

City*:	State*:	ZIP*:
Philadelphia	PA	99999

Patient Agreement

By signing this form, I understand and acknowledge that:

Before my treatment begins, I will:

- Enroll in the SPRAVATO® REMS by completing this *Patient Enrollment Form* with my [illegible] provider. Enrollment information will be submitted to the SPRAVATO® REMS.
- Receive counseling on safety risks and the need for monitoring to obs[illegible]e for [illegible]on of sedation and dissociation, and for any changes in vital signs.

During treatment, and after administration I will:

- Use the SPRAVATO® nasal spray myself under the dir[illegible]t obse[illegible] of a healthcare provider.
- Be observed at the healthcare setting where I [illegible] SPRA[illegible] for at least 2 hours after each treatment until the healthcare provider determines I am ready to leave the healthcare setting.

I understand:

- Sedation and dissociation can [illegible] from treatment with SPRAVATO® and I must stay after each treatment. Until these effects res[illegible]e, I ma[illegible]
  - sleepy and/or
  - disconnected from mys[illegible], my thoughts, feelings and things around me.
- I should make arrangements to safely get home.
- I should not drive or use heavy machinery for the rest of the day on which I receive SPRAVATO®.
- I should contact my doctor or inform him/her at my next visit if I believe I have a side effect or reaction from SPRAVATO®.
- In order to receive SPRAVATO® as an outpatient, I am required to be enrolled in the REMS, and my information will be stored in a database of all outpatients who receive SPRAVATO® in the United States.
- Janssen Pharmaceuticals, Inc. and its agents, including trusted vendors, may contact me or my prescriber via phone, mail, fax, or email to support administration of the REMS.
- Janssen Pharmaceuticals, Inc. and its agents, including trusted vendors, may use, disclose, and share my personal health information for the purpose of the operations of the REMS, including enrolling me into the REMS and administering the REMS, coordinating the dispensing of SPRAVATO®, and releasing and disclosing my personal health information to the Food and Drug Administration (FDA), as necessary, and as otherwise required by law.

Patient Name (please print): Mary Smith

Patient Signature*:	Date*:
	

ANAGEMENT

Date of Birth: 1/1/2000

REMS Status: Enrolled

Most Recent Status Date: 5/23/2018

tment Dosage: 10mg	HCS Location: ABC Location
tment Dosage: 10mg	HCS Location: XYZ Location

nts or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSS
online at www.fda.gov/medwatch.

Spravato® (esketamine) C III nasal spray

MY PATIENTS | CERTIFIED PHARMACIES | DELEGATE MANAGEMENT

Certified Pharmacy Listing

Below is a listing of pharmacies that are REMS-certified and can purchase SPRAVATO®.

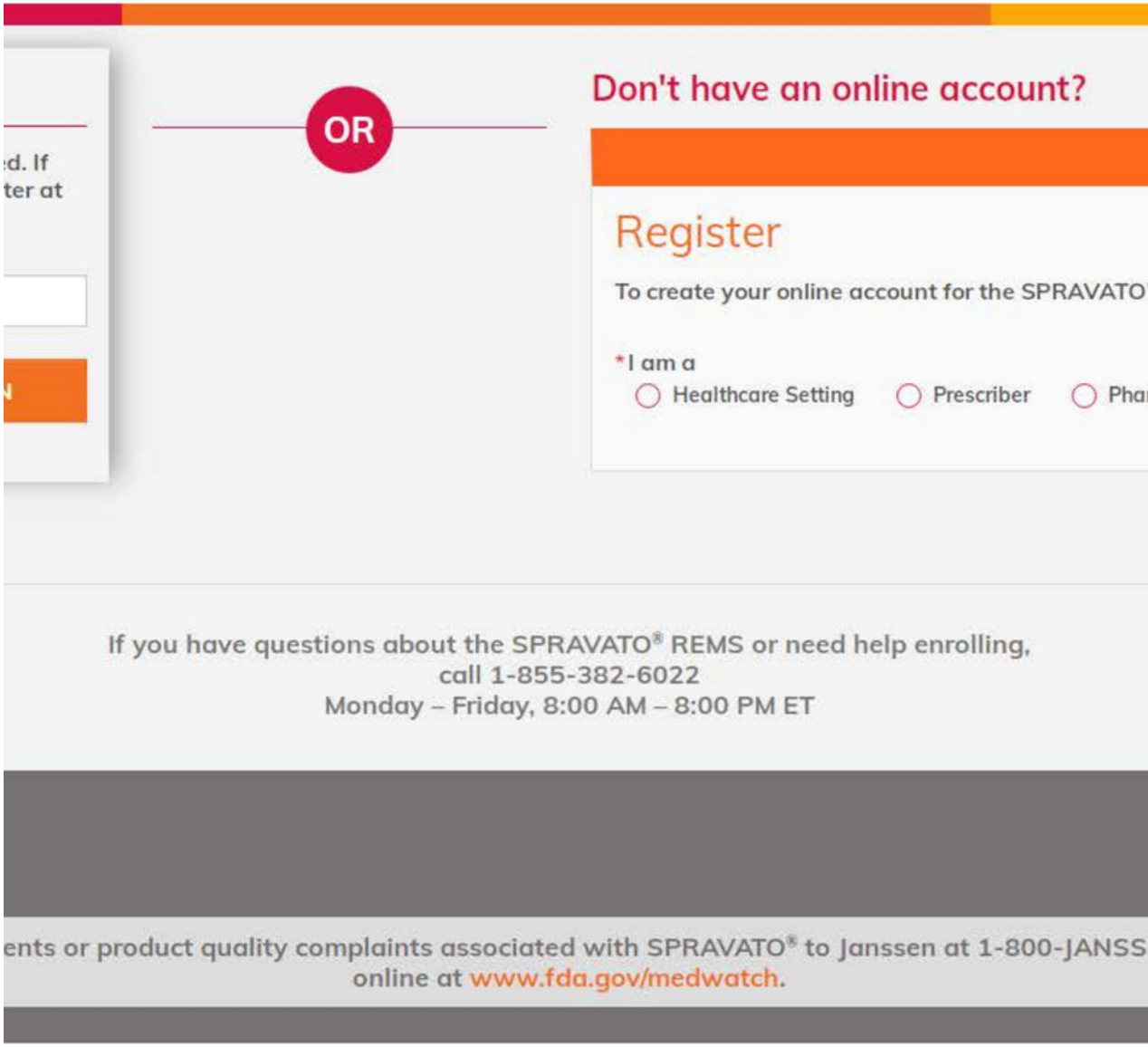
Search/Filter the list by entering information in the textbox below any column header.

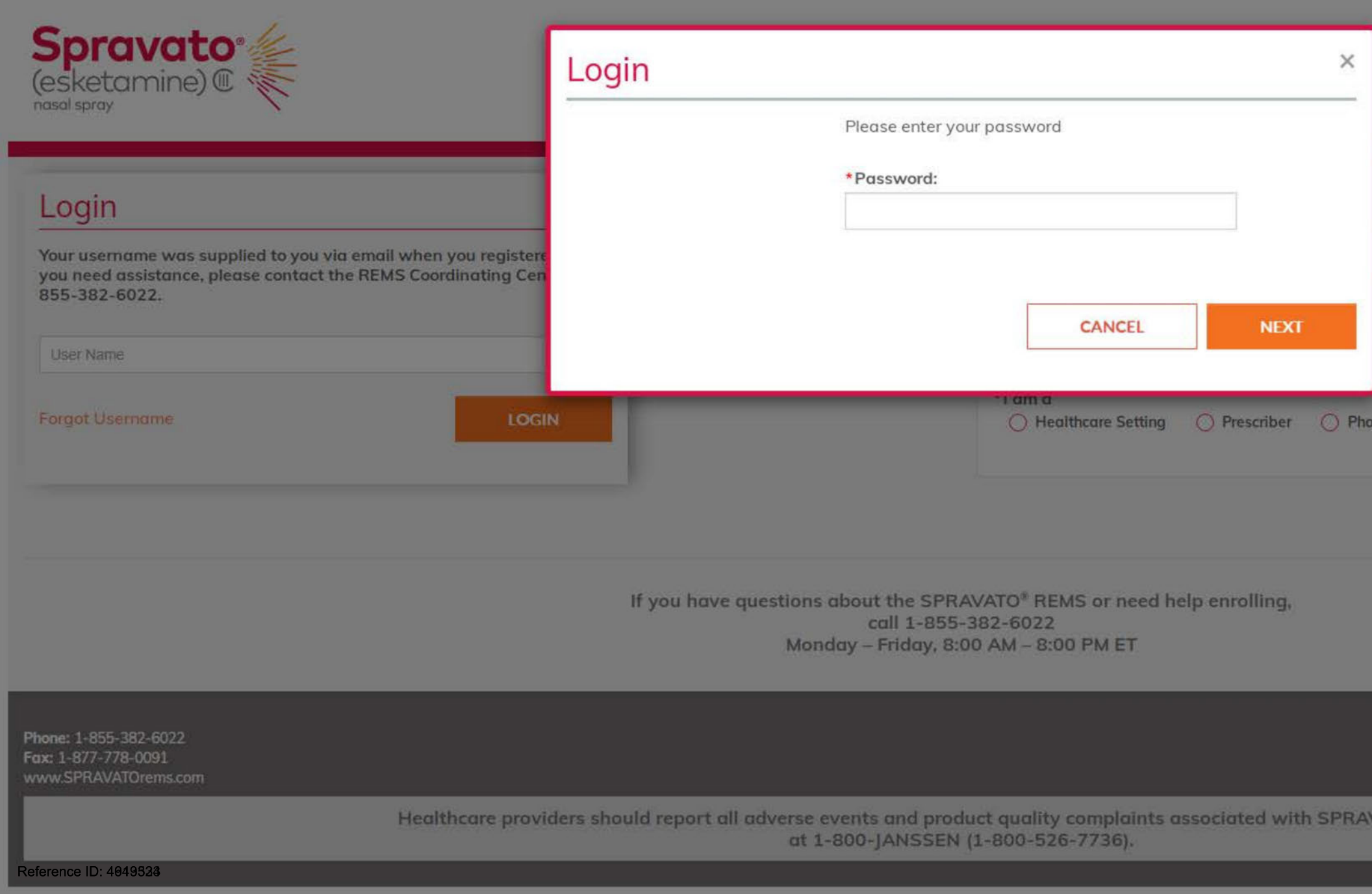
Sort the list by clicking on any column header.

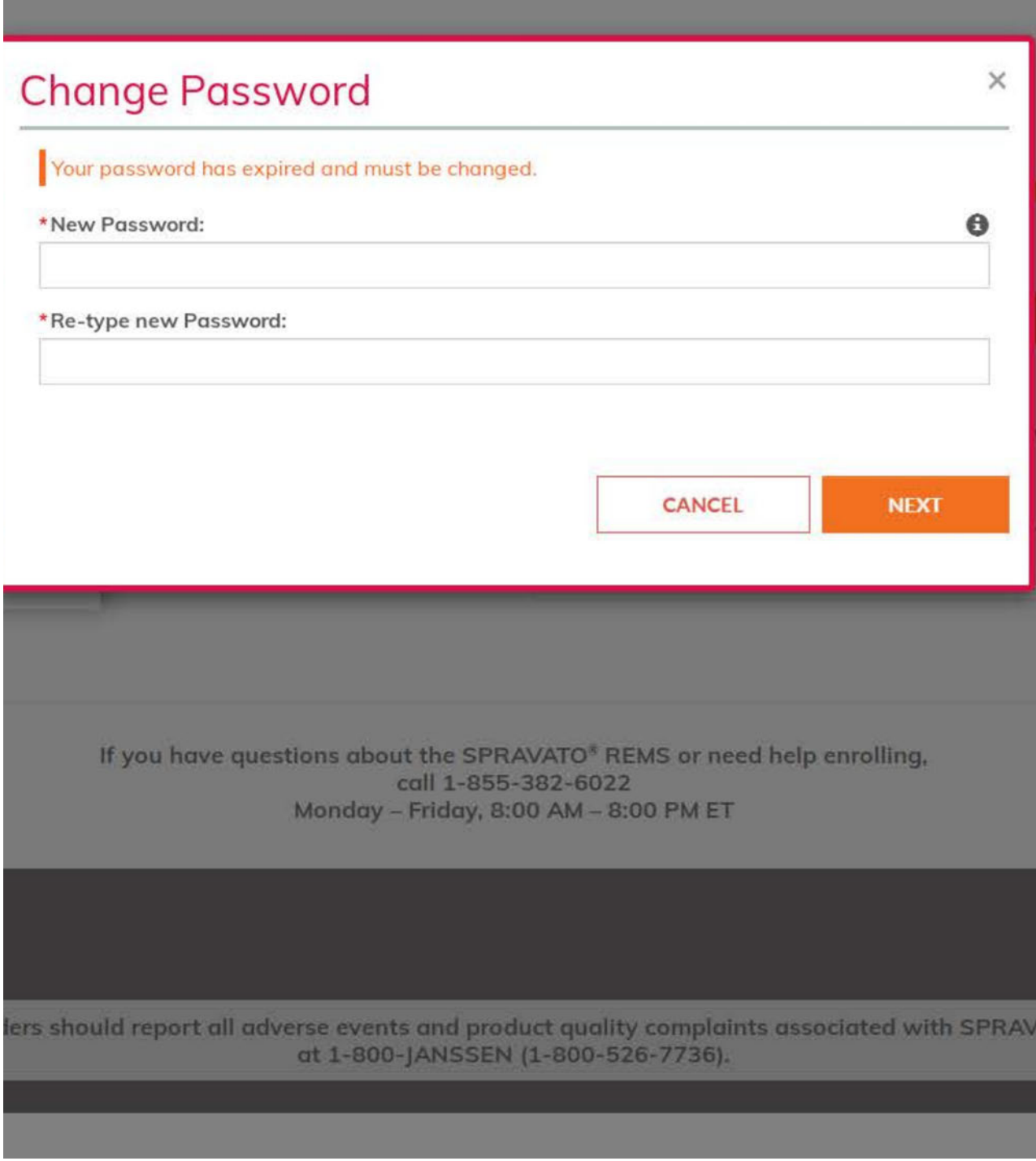
Pharmacy Name	Address 1	Address 2	City	State	Zip
				-- Please Select --	
ABC Pharmacy	100 Main Street	Suite 41	Spicewood	TX	123
XYZ Pharmacy	999 Broadway		Philadelphia	PA	123

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANS
online at www.fda.gov/medwatch.


OR
Don't have an online account?
Register
To create your online account for the SPRAVATO
*I am a
Healthcare Setting
Prescriber
If you have questions about the SPRAVATO® REMS or need help enrolling,
call 1-855-382-6022
Monday – Friday, 8:00 AM – 8:00 PM ET
ents or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSS
online at www.fda.gov/medwatch.


Spravato®
(esketamine) C-III
nasal spray
Login
Your username was supplied to you via email when you registere
you need assistance, please contact the REMS Coordinating Cen
855-382-6022.
User Name
Forgot Username
LOGIN
Login
Please enter your password
*Password:
CANCEL
NEXT
Healthcare Setting
Prescriber
If you have questions about the SPRAVATO® REMS or need help enrolling,
call 1-855-382-6022
Monday – Friday, 8:00 AM – 8:00 PM ET
Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com
Healthcare providers should report all adverse events and product quality complaints associated with SPRA
at 1-800-JANSSEN (1-800-526-7736).


Change Password
Your password has expired and must be changed.
*New Password:
*Re-type new Password:
CANCEL
NEXT
If you have questions about the SPRAVATO® REMS or need help enrolling,
call 1-855-382-6022
Monday – Friday, 8:00 AM – 8:00 PM ET
ers should report all adverse events and product quality complaints associated with SPRAV
at 1-800-JANSSEN (1-800-526-7736).

Spravato® (esketamine) C III nasal spray

Login

Your username was supplied to you via email when you registere
you need assistance, please contact the REMS Coordinating Cen
855-382-6022.

User Name

Forgot Username

LOGI

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com

Healthcare provi

Update Profile









*Security Caption:

*Security Question | *Answer

-- Please Select -- | Answer

-- Please Select -- | Answer

-- Please Select -- | Answer

CANCEL NEXT

Reference ID: 4049523

Spravato® (esketamine) C-III nasal spray

MY PATIENTS | CERTIFIED PHARMACIES

My Patients

Below is a list of your patients.

Patient Listing

- Download the list to spreadsheet format by clicking the Excel icon just above the column headers.
- Search/Filter the list by entering information in the textbox below any column header.
- Sort the list by clicking on any column header.
- Click on Patient REMS ID to view treatment history.

If you w
cannot

Patient REMS ID	First Name	Last Name	Address	City	State	Zip
111111	Robert	Smith	123 Main Street	Philadelphia	PA	19042
22222	Mary	Connors	3 Broadway	Blue Bell	PA	19042

Spravato® (esketamine) C III nasal spray

MY PATIENTS | CERTIFIED PHARMACIES

SPRAVATO® REMS
Patient Monitoring Form - Outpatient Use Only

Instructions

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments.

1. Complete all required fields on this form after **every** treatment session for **all outpatients** enrolled in the SPRAVATO® REMS.
2. Submit completed patient monitoring forms within **7 days**, online at www.SPRAVATOrems.com or by fax (1-877-778-0091).

**Indicates Required Field*

Patient Information

First Name: Peggy
Middle Initial:
Birthdate (MM/DD/YYYY): 1/1/2000
Sex: Female

Concomitant Medications

Is the patient currently taking any of the following medication(s) that may cause sedation or blood pressure cha

*Benzodiazepines
○ Yes ○ No

*Non-benzodiazepine sedative hypnotics
○ Yes ○ No

*Psychostimulants
○ Yes ○ No

*Monoamine oxidase inhibitors (MAOIs)
○ Yes ○ No

Healthcare Provider Conducting Patient Monitoring

*First Name
John

*Last Nam
Smith

*Telephone
555-555-1212

*Email
jsmith@abc

Spravato® (esketamine) C III
nasal spray

MY PATIENTS | CERTIFIED PHARMACIES

SPRAVATO® REMS
Patient Monitoring Form - Outpatient Use Only

Instructions

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments.

1. Complete all required fields on this form after **every** treatment session for **all outpatients** enrolled in the SPRAVATO® REMS.
2. Submit completed patient monitoring forms within **7 days**, online at www.SPRAVATOrems.com or by fax (1-877-778-0091).

**Indicates Required Field*

Patient Information

First Name: Peggy
Middle Initial:
Birthdate (MM/DD/YYYY): 1/1/2000
Sex: Female

Concomitant Medications

Is the patient currently taking any of the following medication(s) that may cause sedation or blood pressure cha

*Benzodiazepines
○ Yes ○ No

*Non-benzodiazepine sedative hypnotics
○ Yes ○ No

*Psychostimulants
○ Yes ○ No

*Monoamine oxidase inhibitors (MAOIs)
○ Yes ○ No

Healthcare Provider Conducting Patient Monitoring

*First Name
John

*Last Nam
Smith

*Telephone

*Email

Spravato® (esketamine) C III nasal spray

MY PATIENTS | CERTIFIED PHARMACIES

Patient Monitoring Form

Thank you for submitting a Patient Monitoring Form for Patient ID 999999.

PRINT/DOWNLOAD | MY PATIENTS

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANS
online at www.fda.gov/medwatch.

Spravato® (esketamine) nasal spray

SPRAVATO® REMS

Patient Monitoring Form - Outpatient Use Only

For Healthcare Setting Use Place Patient Label or Barcode Here

INSTRUCTIONS:

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments.

1. Complete all required fields on this form after **every** treatment session for **all** outpatients enrolled in the SPRAVATO® REMS.
2. Submit completed patient monitoring forms within **7 days**, online at www.SPRAVATOrems.com or by fax (1-877-778-0091).

** Indicates Required Field*

Patient Information (PRINT)

First Name*:	MI:	Last Name*:	Birthdate* (MM/DD/YYYY):	Sex*: ☐ Male ☐ Female ☐ Other

Concomitant Medication

Is the patient currently taking any of the following medication(s) that may cause sedation or blood pressure changes?

- Benzodiazepines* ☐ Yes ☐ No
- Non-benzodiazepine sedative hypnotics* ☐ Yes ☐ No
- Psychostimulants* ☐ Yes ☐ No
- Monoamine oxidase inhibitors (MAOIs)* ☐ Yes ☐ No

Healthcare Provider Conducting Patient Monitoring (PRINT)

First Name*:	Last Name*:
Telephone*:	Email*:

Healthcare Setting Information (PRINT)

Healthcare Setting Name*:		
Healthcare Setting Address 1*:	Healthcare Setting Address 2:	
City*:	State*:	ZIP*:

Patient Treatment Session Information (Administration and Monitoring)

Treatment Date*	Date (MM/DD/YYYY): _____	
Dose Administered*	☐ 56 mg ☐ 84 mg ☐ Other: _____	**Lot Number***: _____
Treatment Duration*	Total time _____ minutes (from 1st device administration to completion of monitoring) Patient must be monitored for at least 2 hours	
REMS Evaluation Question*	*If patient was not for 2-hour minimum monitoring requirement, when would this patient have been ready to leave / no longer require monitoring?* _____ *minutes from start of administration*	
Monitoring of Vital Signs*	Vital signs were in acceptable range **prior** to: • administration? ☐ Yes ☐ No • treatment session completion? ☐ Yes ☐ No	
Monitoring of Blood Pressure*	**Prior to administration** _____/_____ mmHg	**40 mins post-administration** _____/_____ mmHg / **Prior to treatment session completion** _____/_____ mmHg

Did the patient experience Sedation and/or Dissociation

Sedation*: ☐ Yes ☐ No	**Dissociation***: ☐ Yes ☐ No
Onset of symptoms from start of administration* ☐ 1-29 mins ☐ 30-59 mins ☐ 60-89 mins ☐ 90-120 mins ☐ >120 mins	**Onset of symptoms** from start of administration* ☐ 1-29 mins ☐ 30-59 mins ☐ 60-89 mins ☐ 90-120 mins ☐ >120 mins
Resolution of symptoms within 2 hours?* ☐ Yes ☐ No Specify total time to resolution*: _____minutes	**Resolution of symptoms** within 2 hours?* ☐ Yes ☐ No Specify total time to resolution*: _____minutes
Medication(s) given for sedation?* ☐ Yes ☐ No •If YES, name and dose of medication(s): _____	**Medication(s) given for dissociation?*** ☐ Yes ☐ No •If YES, name and dose of medication(s): _____

Spravato® (esketamine) C III
nasal spray

MY PATIENTS | CERTIFIED PHARMACIES

Patient Profile

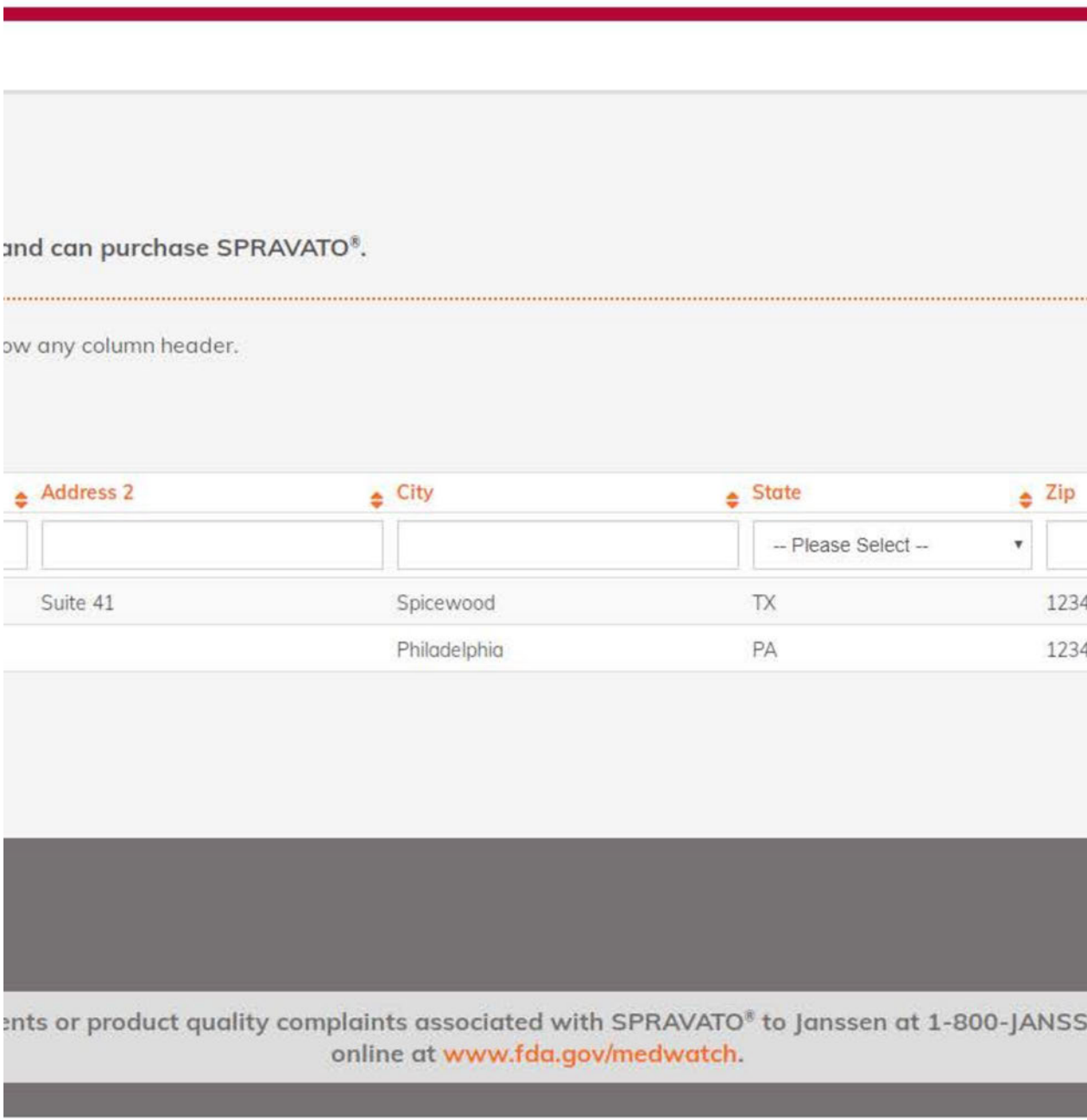
REMS ID: 111111
Robert Smith
123 Main Street
Philadelphia, PA 19042
rsmith@abc.com

Date of Birth: 1/1/2000
REMS Status: Enrolled
Most Recent Status Date: 5/23/2018

Patient Monitoring Forms

Treatment Date: 5/23/2018	**Treatment Dosage:** 10mg	**HCS Location:** ABC Location
Treatment Date: 3/23/2018	**Treatment Dosage:** 10mg	**HCS Location:** XYZ Location

Phone: 1-855-382-6022
Fax: 1-877-778-0091
www.SPRAVATOrems.com


and can purchase SPRAVATO®.
ow any column header.
Address 2
City
State
Zip
-- Please Select --
Suite 41
Spicewood
TX
1234
Philadelphia
PA
1234
nts or product quality complaints associated with SPRAVATO® to Janssen at 1-800-JANSS
online at www.fda.gov/medwatch.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211243Orig1s006

RISK ASSESSMENT AND RISK MITIGATION REVIEW(S)

Division of Risk Management (DRM)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Application Type	NDA
Application Number	211243
Supplement Number, Date Recieved	Supplment 6, Received October 11, 2021 (Sequence 0235)
Action Date	December 29, 2021
OSE RCM #	2021-2014
Reviewer Name	Somya Dunn, MD
Team Leader	Carolyn Tieu, Pharm.D., MPH
Division Director	Cynthia LaCivita, Pharm.D.
Review Completion Date	December 29, 2021
Subject	Review of proposed Minor REMS Modification
Established Name	estketamine
Trade Name	Spravato
Name of Applicant	Janssen Pharmaceuticals, Inc.
Therapeutic Class	N-methyl-D-aspartate glutamate (NMDA) receptor antagonist
Formulation(s)	Nasal spray

ADDENDUM TO REMS REVIEW

This is an addendum to the REMS review dated December 14, 2021, for the proposed minor modification to the risk evaluation and mitigation strategy (REMS) for Spravato (esketamine nasal spray), new drug application (NDA) 211243, Supplement 6. This Supplement was submitted by Janssen Pharmaceuticals, Inc (Applicant) on October 11, 2021 and amended on November 17, 2021. Two of the dates listed in the review were incorrect:

- One error stated that Supplement 6 was received on October 12, 2021; it was received on October 11, 2021.
- The timetable for submission of assessments of the REMS was stated to remain the same as that approved on March 6, 2019; the actual approval date was March 5, 2019.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SOMYA V DUNN
12/29/2021 05:13:25 PM

CYNTHIA L LACIVITA
01/02/2022 09:41:04 PM

Division of Risk Management (DRM)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Application Type	NDA
Application Number	211243
Supplement Number, Date Recieved	Supplment 6, Received October 12, 2021 (Sequence 0235)
Action Date	December 15, 2021
OSE RCM #	2021-2014
Reviewer Name	Somya Dunn, MD
Team Leader	Carolyn Tieu, Pharm.D., MPH
Division Director	Cynthia LaCivita, Pharm.D.
Review Completion Date	December 14, 2021
Subject	Review of proposed Minor REMS Modification
Established Name	estketamine
Trade Name	Spravato
Name of Applicant	Janssen Pharmaceuticals, Inc.
Therapeutic Class	N-methyl-D-aspartate glutamate (NMDA) receptor antagonist
Formulation(s)	Nasal spray

TABLE OF CONTENTS

APPEARS THIS WAY ON ORIGINAL

1. INTRODUCTION

This review evaluates the proposed minor modification to the risk evaluation and mitigation strategy (REMS) for Spravato (esketamine nasal spray), new drug application (NDA) 211243, submitted by Janssen Pharmaceuticals, Inc (Applicant) on October 12, 2021 and amended on November 17, 2021. The Applicant proposed changes to the Spravato REMS Patient Monitoring Form, including revising the format of some of the data-capturing fields and adding a field to capture the lot number field of Spravato. These changes do not affect the risk message or change the REMS requirements.

1.1 PRODUCT INFORMATION

Spravato (esketamine nasal spray) is the S-enantiomer of ketamine, an N-methyl-D-aspartate glutamate (NMDA) receptor antagonist that enhances glutamine release in the brain, approved for the treatment of treatment-resistant depression. Spravato is a drug-device combination of esketamine designed for intranasal administration.

Spravato was approved on March 5, 2019 with a REMS to ensure the benefits of the drug outweigh the increased risks of misuse, abuse and serious adverse outcomes from sedation and dissociation.[1]

The goal of the REMS is to mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by Spravato administration, and abuse and misuse of Spravato by:

- Ensuring that Spravato is only dispensed and administered to patients in a medically supervised healthcare setting that monitors these patients
- Ensuring pharmacies and healthcare settings that dispense Spravato are certified
- Ensuring that each patient is informed about the serious adverse outcomes resulting from sedation and dissociation and need for monitoring
- Enrollment of all patients in a registry to further characterize the risks and support safe use

The most recently approved REMS (approved July 31, 2020) for Spravato consists of elements to assure safe use, implementation system, and a timetable for submission of assessments for the REMS. The elements to assure safe use include healthcare setting certification, pharmacy certification, safe use conditions, patient monitoring and patient registry

1.2 REGULATORY HISTORY

The regulatory history relevant to the proposed REMS modification is summarized below:

- 10/12/2021: The Applicant submitted a proposed minor REMS modification (EDR Sequence 0235).
- 11/8/2021: The Agency requested that the Applicant submit the full REMS to Supplement 6.
- 11/17/2021: The Applicant submitted an amendment to Supplement 6; the full REMS as requested by the Agency (EDR Sequence 0252).

2. REVIEW OF PROPOSED REMS MODIFICATIONS

The Applicant did not propose changes to the goals or requirements.

2.1 REMS PARTICIPANTS REQUIREMENTS AND MATERIALS

Only the particiant's associated material that is impacted by this minor modification are included below.

2.1.1 Healthcare Provider

The Applicant proposed changes to the Patient Monitoring Form to include:

- Addition of the lot number field
- Bolding the minutes (units of measure) for Treatment Duration, REMS Evaluation Question and Resolution of Symptoms for Dissociation/Sedation.
- Addition of the treatment date on page 2 in the event forms are faxed in separately (out of sequence)
- Adding a "/" in the middle of each blank line for blood pressure capture

Reviewer Comment: *We agree with these proposed changes; none of the proposed changes affect the risk message.*

2.2 REMS APPLICANT REQUIREMENTS AND MATERIALS

2.2.1 Operations

The Applicant did not propose changes to the website, but the appended *Patient Monitoring Form* was updated with the proposed changes described in Section 2.1.1.

Reviewer Comment*: The proposed screen shots capture the update and are acceptable.*

2.3 TIMETABLE FOR SUBMISSION OF ASSESSMENTS

The timetable for submission of assessments of the REMS will remain the same as that approved on March 6, 2019.

2.4 SUPPORTING Document

The Applicant did not propose any changes to the Supporting Document.

2.5 REMS ASSESSMENT PLAN

There are no changes to the REMS Assessment Plan described in the July 31, 2020 Supplement 4 approval letter.[1]

3. DISCUSSION

In the proposed REMS minor modification submitted on October 12, 2021, the Applicant made format and editorial changes and revisions to the Spravato REMS Patient Monitoring Form. All of the proposed changes are to clarify and improve the information requested on the forms. No other changes were proposed to the REMS for Spravato and the proposed changes do not affect the risk message or the REMS requirements.

4. CONCLUSION AND RECOMMENDATIONS

DRM finds the proposed REMS minor modification for Spravato (esketamine nasal spray) submitted on October 12, 2021 and amended on November 17, 2021 to be acceptable.

The timetable for the submission of assessments of the REMS will remain the same as that approved on March 6, 2019.

The REMS assessment plan is not changing and will remain the same as that that described in the July 31, 2020 Approval letter.

5. REFERENCES

[1] Spravato Supplement 4 Approval Letter, July 31, 2020.

6. APPENDICES

REMS Document
Outpatient Healthcare Setting Enrollment Form
Inpatient Healthcare Setting Enrollment Form
Patient Enrollment Form
Pharmacy Enrollment Form
REMS Program Overview
Patient Monitoring Form
REMS Program Website

105 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SOMYA V DUNN
12/14/2021 01:57:52 PM

CAROLYN N TIEU
12/14/2021 02:20:55 PM

CYNTHIA L LACIVITA
12/14/2021 02:29:59 PM