

Risk Evaluation and Mitigation Strategy (REMS) Document

DSUVIA™ (sufentanil) REMS Program

I. Administrative Information

Application Number: NDA 209128
Application Holder: AcclRx Pharmaceuticals, Inc.
Initial REMS Approval: 11/2018

II. REMS Goal

The goal of the DSUVIA REMS is to mitigate the risk of respiratory depression resulting from accidental exposure by:

- Ensuring that DSUVIA is dispensed only to patients in certified medically supervised healthcare settings.

III. REMS Requirements

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

1. Healthcare settings that dispense DSUVIA must:

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- | | |
|---------------------------------|--|
| To become certified to dispense | <ol style="list-style-type: none">1. Be able to manage acute opioid overdose, including respiratory depression.2. 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.3. Have the authorized representative enroll in the REMS Program by completing the Healthcare Setting Enrollment Form and submitting it to the REMS Program.4. Train all relevant staff that DSUVIA must not be dispensed for use outside of the certified healthcare setting.5. Train all relevant staff involved in administration of DSUVIA to refer to the Directions for Use prior to administration.6. Establish processes and procedures to verify that DSUVIA is not dispensed for use outside of the certified healthcare setting. |
|---------------------------------|--|

To maintain certification to dispense	7. Have a new authorized representative enroll in the REMS Program by completing the Healthcare Setting Enrollment Form if the authorized representative changes.
At all times	8. Not dispense DSUVIA for use outside the certified healthcare setting. 9. Not distribute, transfer, loan or sell DSUVIA. 10. Maintain records of staff training. 11. Maintain records of all processes and procedures including compliance with those processes and procedures. 12. Comply with audits by AcelRx Pharmaceuticals, Inc. or a third party acting on behalf of AcelRx Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

2. Wholesalers-distributors that distribute DSUVIA must:

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

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

1. Establish and maintain a REMS Program website, www.DSUVIAREMS.com. The REMS Program website must include the capability to complete healthcare setting certification online and, the option to print the Prescribing Information, Directions for Use, 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.
2. Make the REMS Program website fully operational and all REMS materials available through website and call center by the date DSUVIA is first commercially distributed.
3. Establish and maintain a REMS Program call center for REMS participants at 1-855-925-8476.

4. Establish and maintain a validated, secure database of all REMS participants who are certified in the DSUVIA REMS.
5. Ensure healthcare settings are able to enroll by fax, mail, and online.
6. Provide [Healthcare Setting Enrollment Form](#) and the Prescribing Information to healthcare settings that (1) attempt to order DSUVIA and are not yet certified or (2) inquire about how to become certified.
7. Notify healthcare settings, confirming certification, within 7 calendar days after they become certified in the REMS Program.
8. Provide wholesalers-distributors access to the database of certified healthcare settings.

To ensure REMS participants' compliance with the REMS Program, AcelRx Pharmaceuticals, Inc. must:

9. Verify annually that the authorized representative's name and contact information correspond to those of the current designated authorized representative for the healthcare setting. If different, the healthcare setting must be required to re-certify with a new authorized representative.
10. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: DSUVIA distribution; certification of healthcare settings; and audits of REMS participants.
11. Establish a plan for addressing noncompliance with REMS Program requirements.
12. Monitor healthcare settings and wholesaler-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.
13. Audit all certified healthcare settings at 6 months and 12 months from the date the drug is first commercially distributed, and annually thereafter to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements. To be audited, healthcare settings must have received at least one shipment of DSUVIA in the past 6 months.
14. Audit wholesalers-distributors no later than 90 calendar days after they become authorized to distribute the drug or from the date DSUVIA is first commercially distributed (whichever is later) to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements.
15. Take reasonable steps to improve operation of and compliance with the requirements in the DSUVIA REMS Program based on monitoring and evaluation of the DSUVIA REMS Program.

IV. REMS Assessment Timetable

AcelRx Pharmaceuticals, Inc. must submit REMS Assessments at 6 months, 12 months, and annually thereafter from the date of the initial approval of the REMS (11/02/2018). 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. AcelRx 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 DSUVIA REMS:

Enrollment Forms

Healthcare Setting:

1. [Healthcare Setting Enrollment Form](#)

Other Materials

2. [REMS Program Website](#)

DSUVIA (sufentanil sublingual tablet 30 mcg) is only available through the DSUVIA Risk Evaluation and Mitigation Strategy (REMS). DSUVIA can only be dispensed and/or administered in healthcare settings that are enrolled in the REMS.

To enroll your healthcare setting,

- 1) Designate an Authorized Representative (e.g. Pharmacy and Therapeutics Chair, Pharmacy Director, Medical Director, Medical Chief-of-Staff, Director of Nursing, etc.)
- 2) Complete, sign, and submit this **Healthcare Setting Enrollment Form** to the DSUVIA REMS.

Once your healthcare setting is officially enrolled, a notification will be provided to the Authorized Representative.

HEALTHCARE SETTING AGREEMENT

I am the Authorized Representative designated by my healthcare setting to coordinate the certification process and oversee implementation of and compliance with the REMS. By signing this form, I agree to comply, on behalf of my healthcare setting, with the following REMS requirements:

- I am authorized to complete the **Healthcare Setting Enrollment Form** and submit it to the REMS Program on behalf of this healthcare setting.
- This healthcare setting is able to manage acute opioid overdose, including respiratory depression.
- This healthcare setting must not dispense DSUVIA for outpatient use.
 - Train all relevant staff that DSUVIA must not be dispensed for use outside of this healthcare setting.
 - Establish processes and procedures to verify that DSUVIA is not dispensed for use outside of this healthcare setting.
- This healthcare setting must train all relevant staff involved in administration of DSUVIA to read the Directions for Use prior to administering DSUVIA.
- This healthcare setting must not distribute, transfer, loan, or sell DSUVIA.
- This healthcare setting must maintain records of staff training and of all processes and procedures including compliance with those processes and procedures.
- This healthcare setting must comply with audits by AcelRx Pharmaceuticals, Inc. or a third party acting on behalf of AcelRx Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed for the DSUVIA REMS. Failure to comply may result in decertification of the healthcare setting.
- If the Authorized Representative changes, this healthcare setting will have a new Authorized Representative enroll in the REMS by completing the **Healthcare Setting Enrollment Form**.

AUTHORIZED REPRESENTATIVE INFORMATION

Signature: _____ Date: _____

Printed Name, Credentials: _____ Title: _____

Phone Number: _____ Fax Number: _____

Email Address: _____ Preferred Method of Communications: EMAIL FAX

HEALTHCARE SETTING INFORMATION

Name: _____

Street Address: _____ City: _____

State: _____ ZIP: _____ DEA License Number: _____

SUBMIT BY MAIL:

AcelRx Pharmaceuticals, Inc. 351 Galveston Drive
Attn: REMS Administrator Redwood City, CA 94063

OR

BY EMAIL:

DSUVIAREMS@acelrx.com

OR

BY FAX:

1-650-649-1855

If you have any questions or require additional information or further copies of DSUVIA REMS materials, please visit www.DSUVIAREMS.com, or contact the DSUVIA REMS at:

AcelRx Pharmaceuticals, Inc.
Attn: REMS Administrator
351 Galveston Drive
Redwood City, CA 94063

Phone: 1-855-925-8476
Email: DSUVIAREMS@acelrx.com
Fax: (650) 649-1855

This form is part of an FDA-approved REMS.
For more information about DSUVIA, please see Prescribing Information, including Boxed Warnings.

Risk Evaluation and Mitigation Strategy (REMS)

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

A REMS is a strategy to manage known or potential serious risks associated with a drug and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug outweigh its risks. **DSUVIA is intended for sublingual delivery only by a healthcare provider.** DSUVIA is available only through a restricted distribution strategy called the DSUVIA REMS in order to prevent **respiratory depression resulting from accidental exposure.**

What are the DSUVIA REMS requirements?

Healthcare settings that dispense DSUVIA must:

To become certified to dispense

1. Be able to manage acute opioid overdose, including respiratory depression.
2. 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.
3. Have the Authorized Representative enroll in the REMS Program by completing the **Healthcare Setting Enrollment Form** and submitting it to the REMS Program.
4. Train all relevant staff that DSUVIA must not be dispensed for use outside of the certified healthcare setting.
5. Train all relevant staff involved in administration of DSUVIA to refer to the Directions for Use prior to administration.
6. Establish processes and procedures to verify that DSUVIA is not dispensed for use outside of the certified healthcare setting.

To maintain certification to dispense

7. Have a new Authorized Representative enroll in the REMS Program by completing the **Healthcare Setting Enrollment Form** if the Authorized Representative changes.

At all times

8. Not dispense DSUVIA for use outside the certified healthcare setting.
9. Not distribute, transfer, loan, or sell DSUVIA.
10. Maintain records of staff training.
11. Maintain records of all processes and procedures including compliance with those processes and procedures.
12. Comply with audits by AcelRx Pharmaceuticals, Inc. or a third party acting on behalf of AcelRx Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

DSUVIA Healthcare Setting Enrollment Form

Download and complete the enrollment form to submit it 1 of 3 ways:

- **By email:** DSUVIAREMS@acelrx.com
- **By fax:** 1-650-649-1855
- **By mail:** AcelRx Pharmaceuticals, Inc.
Attn: REMS Administrator
351 Galveston Drive
Redwood City, CA 94063

DOWNLOAD FORM

Complete and submit the enrollment form online.

ENROLL ONLINE

How does my healthcare setting become certified in the DSUVIA REMS?

Your healthcare setting must designate an Authorized Representative to coordinate the certification process and oversee implementation of and compliance with the DSUVIA REMS. To enroll your healthcare setting, the Authorized Representative must complete, sign, and submit the **Healthcare Setting Enrollment Form** to the DSUVIA REMS.

By signing the **Healthcare Setting Enrollment Form**, the Authorized Representative agrees to comply, on behalf of your healthcare setting, with the following REMS requirements:

- He/she is authorized to complete the **Healthcare Setting Enrollment Form** and submit it to the REMS Program on behalf of your healthcare setting
- Your healthcare setting is able to manage acute opioid overdose, including respiratory depression
- Your healthcare setting must not dispense DSUVIA for outpatient use
 - Train all relevant staff that DSUVIA must not be dispensed for use outside of the healthcare setting
 - Establish processes and procedures to verify that DSUVIA is not dispensed for use outside of your healthcare setting
- Your healthcare setting must train all relevant staff involved in administration of DSUVIA to read the Directions for Use prior to administering DSUVIA
- Your healthcare setting must not distribute, transfer, loan, or sell DSUVIA
- Your healthcare setting must maintain records of staff training and of all processes and procedures including compliance with those processes and procedures
- Your healthcare setting must comply with audits by AcelRx Pharmaceuticals, Inc. or a third party acting on behalf of AcelRx Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed for the DSUVIA REMS. Failure to comply may result in decertification of the healthcare setting
- If the Authorized Representative changes, your healthcare setting will have a new Authorized Representative enroll in the REMS by completing the **Healthcare Setting Enrollment Form**

Receive On-Site Medical Information

AcelRx Pharmaceuticals, Inc. will provide information on DSUVIA at certified healthcare settings upon request.



To make an appointment, call
1-855-925-8476

This phone number is also available for reporting product complaints.

Healthcare Setting Resources

DSUVIA is only available through the DSUVIA Risk Evaluation and Mitigation Strategy (REMS) developed by AcelRx. Healthcare settings must enroll in the DSUVIA REMS to become certified to dispense DSUVIA. This section includes important product information.

Product Information:

DSUVIA
Directions for Use

DOWNLOAD

Prescribing
Information

DOWNLOAD

Healthcare Setting
Enrollment Form

DOWNLOAD

Indication

DSUVIA contains sufentanil, an opioid agonist, and is indicated for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

- Not for home use or for use in children. Discontinue treatment with DSUVIA before patients leave the certified medically supervised healthcare setting.
- Not for use for more than 72 hours.
- Only to be administered by a healthcare provider.
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve DSUVIA for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combination products]:
 - Have not been tolerated, or are not expected to be tolerated,
 - Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Adverse Reaction Reporting:

AcelRx Pharmaceuticals, Inc. is committed to patient safety. To report suspected adverse reactions with DSUVIA, please contact:

AcelRx Pharmaceuticals, Inc.
1-855-925-8479

Food and Drug Administration (FDA)
1-800-FDA-1088

or visit
www.fda.gov/medwatch

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- If the Authorized Representative changes, this healthcare setting will have a new Authorized Representative enroll in the REMS by completing the **Healthcare Setting Enrollment Form**.

AUTHORIZED REPRESENTATIVE INFORMATION

Signature: _____ Date: _____

Printed Name, Credentials: _____ Title: _____

Phone Number: _____ Fax Number: _____

Email Address: _____ Preferred Method of Communications: EMAIL FAX

HEALTHCARE SETTING INFORMATION

Name: _____

Street Address: _____ City: _____

State: _____ ZIP: _____ DEA License Number: _____

SUBMIT BY MAIL:

AcelRx Pharmaceuticals, Inc. 351 Galveston Drive
Attn: REMS Administrator Redwood City, CA 94063

OR

BY EMAIL:

DSUVIAREMS@acelrx.com

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Please Review & Act on These Documents



Sample Sender
REMS Enrollment Form

Please review & sign your document. To begin the process of reviewing and signing your documents, please click the button below. Signing will not be complete until you have reviewed the agreement and you have confirmed your signature.

Please review the documents below.

CONTINUE

OTHER ACTIONS ▾

DSUVIA™ REMS

Healthcare Setting Enrollment Form

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- If the Authorized Representative changes, this healthcare setting will have a new Authorized Representative enroll in the REMS by completing the **Healthcare Setting Enrollment Form**.

AUTHORIZED REPRESENTATIVE INFORMATION



START

DSUVIA™ REMS

Healthcare Setting Enrollment Form

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AUTHORIZED REPRESENTATIVE INFORMATION

Signature: _____		Date: _____
Printed Name, Credentials: _____	Title: _____	
Phone Number: _____	Fax Number: _____	
Email Address: _____	Preferred Method of Communications: <input type="checkbox"/> EMAIL <input type="checkbox"/> FAX	

HEALTHCARE SETTING INFORMATION

Name: _____		
Street Address: _____	City: _____	
State: _____	ZIP: _____	DEA License Number: _____

Page 1 of 2

NEXT



START

DSUVIA™ REMS

Healthcare Setting Enrollment Form

SUBMIT BY MAIL:

AcelRx Pharmaceuticals, Inc. 351 Galveston Drive
Attn: REMS Administrator Redwood City, CA 94063

OR

BY EMAIL:

DSUVIAREMS@acelrx.com

OR

BY FAX:

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FINISH

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/

JOSHUA M LLOYD on behalf of SHARON H HERTZ
11/02/2018