CENTER FOR DRUG EVALUATION AND RESEARCH

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REMS

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NDA 022569
Lazanda (fentanyl) [NASAL SPRAY]
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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goals of the Lazanda (fentanyl) nasal spray REMS are to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors by:

1. Prescribing and dispensing Lazanda only to appropriate patients, which includes use only in opioid-tolerant patients

2. Preventing inappropriate conversion between fentanyl products

3. Preventing accidental exposure to children and others for whom it was not prescribed

4. Educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose

II. REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each Lazanda prescription in accordance with 21 CFR § 208.24.

The Medication Guide is part of the REMS and is appended.

B. Elements to Assure Safe Use (ETASU)

1. Healthcare providers who prescribe Lazanda for <u>outpatient</u> use are specially certified.

a. Archimedes Development Limited (Archimedes) will ensure that healthcare providers who prescribe Lazanda for outpatient use are specially certified.

b. To become certified to prescribe Lazanda, prescribers will be required to enroll in the Lazanda REMS program. Prescribers must complete the following requirements to be enrolled:

i. Review the Lazanda REMS prescriber educational materials (*Prescriber Education Program)*, including the Full Prescribing Information, and successfully complete the knowledge assessment (*Prescriber Knowledge Assessment*).

ii. Complete and sign the *Prescriber Enrollment Form*. In signing the Prescriber Enrollment Form, each prescriber is required to acknowledge the following:

a) I understand the responsible use conditions for Lazanda and the risks and benefits of chronic opioid therapy.

b) I understand that Lazanda can be abused, and that this risk should be considered when prescribing or dispensing Lazanda in situations where I

am concerned about an increased risk of misuse, abuse, or overdose, whether accidental or intentional.

c) I understand that Lazanda is indicated only for the management of breakthrough pain in patients with cancer, who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

d) I understand that Lazanda is contraindicated for use in opioid non-tolerant patients, and know that fatal overdose can occur at any dose.

e) I understand that Lazanda must not be used to treat any contraindicated conditions such as acute or postoperative pain, including headache/migraine.

f) I understand that the initial starting dose of Lazanda for all patients is the lowest dose (100mcg), and that patients must be titrated individually.

g) I understand that Lazanda is not bioequivalent with any other fentanyl product (regardless of route of administration), and that substitution may result in fatal overdose. I understand that patients switching from another fentanyl product to Lazanda must not be converted on a microgram-per-microgram basis.

h) I will complete and sign a Lazanda REMS *Patient-Prescriber Agreement* with each new patient, before writing the patient's first prescription, and re-new the agreement every two (2) years.

In signing the *Patient-Prescriber Agreement*, the prescriber documents the following:

1) Patient is currently using around-the-clock opioid analgesia and has been for at least one (1) week.

2) Patient is opioid tolerant. Patients considered opioid tolerant are those who are regularly taking at least: 60 mg oral morphine/day; 25 micrograms transdermal fentanyl/hour; 30 mg oral oxycodone/day; 8 mg oral hydromorphone/day; 25 mg oral oxymorphone/day; or an equianalgesic dose of another opioid for one (1) week or longer.

3) The Lazanda Medication Guide has been provided to and reviewed with the patient or their caregiver.

4) The patient or their caregiver has been counseled about the risks, benefits, and appropriate use of Lazanda including communication of the following safety messages:

A. If patients stop taking their around-the-clock opioid medication, they must stop taking Lazanda.

B. NEVER share Lazanda.

C. Giving Lazanda to someone for whom it has not been prescribed can result in a fatal overdose.

D. Lazanda can be fatal to a child; used and unused dosage units must be safely stored out of the reach of children living in or likely to visit the home.

In signing the *Patient-Prescriber Agreement,* the patient and/or their caregiver document the following:

1) My prescriber has given me a copy of the Lazanda Medication Guide and has reviewed it with me.

2) I understand that before I can take Lazanda, I must be regularly using another opioid pain medicine, around-the clock, for my constant pain.

3) I understand that if I stop taking my around-the-clock opioid pain medicine for my constant pain, I must stop taking Lazanda.

4) I understand how I should take Lazanda, including how much I can take, and how often I can take it.

5) I understand that Lazanda can cause serious side effects, including life-threatening breathing problems which can lead to death, especially if I do not take Lazanda exactly as my prescriber has directed me to take it.

6) I agree to contact my prescriber if Lazanda does not relieve my pain. I will not change my dose of Lazanda myself or take Lazanda more often than my prescriber has directed.

7) I agree that I will never give Lazanda to anyone else, even if they have the same symptoms, since it may harm them or even cause death.

8) I will store Lazanda in a safe place away from children and teenagers because accidental use by a child, or anyone for whom it was not prescribed, is a medical emergency and can cause death.

9) I have been instructed on how to properly dispose of unused and remaining Lazanda and will dispose of Lazanda as soon as I no longer need it.

10) I understand that selling or giving away Lazanda is against the law.

11) I have asked my prescriber all the questions I have about Lazanda. If I have any additional questions or concerns in the future about my treatment with Lazanda, I will contact my prescriber.

12) I have reviewed the Patient Authorization for Disclosure and Use of Health Information for Lazanda REMS Statement and I agree to its terms and conditions which authorize my healthcare providers and health plans to disclose my personal and medical information to Archimedes, (the maker of Lazanda) and their agents and contractors, to administer the REMS program.

i) I will provide a completed, signed copy of the *Patient-Prescriber Agreement* to the patient and retain a copy for my records. I will also provide a completed, signed copy to the Lazanda REMS program (by fax, or through the *Lazanda REMS website*) within ten (10) working days.

j) At all follow-up visits, I agree to assess the patient for appropriateness of the dose, and for signs of misuse and abuse.

k) I understand that Lazanda is only available through the Lazanda REMS program. I understand and agree to comply with the Lazanda REMS program requirements for prescribers.

b. Prescribers are required to re-enroll every two (2) years. Additionally, prescribers must re-counsel their patients and complete a new Patient-Prescriber Agreement at least every two (2) years.

c. Archimedes will:

i. Ensure that prescriber enrollment can successfully be completed via the Lazanda REMS website, mail, fax, or by scanning and e-mailing the forms.

ii. Ensure that, as part of the enrollment process, prescribers receive the following materials that are part of the Lazanda REMS program and are appended:

• *The Lazanda REMS Program Overview (Prescribers)*

• *Prescriber Education Program*

• *Prescriber Knowledge Assessment*

• *Prescriber Enrollment Form*

• *Patient-Prescriber Agreement*

• *Lazanda REMS website*

iii. Ensure that prescribers have successfully completed the knowledge assessment, and ensure that enrollment forms are complete before activating a prescriber's enrollment in the Lazanda REMS program.

iv. Ensure that prescribers are notified when they are successfully enrolled in the Lazanda REMS program, and therefore, are certified to prescribe Lazanda.

v. Monitor education and enrollment requirements for prescribers and may inactivate non-compliant prescribers. Upon initial activation, prescribers remain active until inactivation occurs or expiration of the enrollment period.

vi. Ensure that at least 2 weeks prior to first availability of Lazanda to healthcare providers, a Dear Healthcare Provider Letter will be sent. The target audience for the letter will include pain management specialists (comprised of anesthesiologists, physical medicine and rehabilitation physicians and primary care physicians), oncologists, oncology nurse practitioners who treat breakthrough pain in patients with cancer, and other appropriately licensed healthcare professionals who prescribe transmucosal fentanyl products. The letter will include information on the risks associated with the use of Lazanda and will explain to healthcare providers that if they wish to treat patients using Lazanda, they must enroll in the Lazanda REMS program. The letter will be accompanied by a copy of the Full Prescribing Information (which will include the Medication Guide), and will be available on the Lazanda REMS website for 1 year from the date of the mailing.

The *Dear Healthcare Provider Letter* is part of the Lazanda REMS Program and is appended.

2. Lazanda will only be dispensed by pharmacies that are specially certified

a. Archimedes will ensure that Lazanda will only be dispensed by certified pharmacies. To become certified to dispense Lazanda, each pharmacy must be enrolled in the Lazanda REMS program.

b. Each pharmacy will be required to designate an authorized pharmacist to complete enrollment on behalf of the pharmacy.

c. There is a different set of enrollment requirements for outpatient pharmacies (e.g., retail, mail order, institutional outpatient pharmacies that dispense for outpatient use) and inpatient pharmacies (e.g., hospitals, hospices, and long-term care facilities that dispense for inpatient use).

d. ***Outpatient Pharmacies:***

The authorized pharmacist must complete the following requirements to enroll their **outpatient pharmacy**:

i. Review the Lazanda REMS education program (*Pharmacy Education Program*) and successfully complete the *Pharmacy Knowledge Assessment.*

ii. Ensure the pharmacy enables their pharmacy management system to support communication with the Lazanda REMS system, using established telecommunication standards, and runs the standardized validation test transaction to validate the system enhancements.

iii. Complete and sign the *Pharmacy Enrollment Form[Outpatient Pharmacy or Chain Pharmacy Enrollment Form, as applicable]*. In signing the *Pharmacy Enrollment Form*, the authorized pharmacist is required to acknowledge the following:

a) I understand the risks and benefits associated with Lazanda and the requirements of the Lazanda REMS program for pharmacies.

b) I will ensure that all pharmacy staff who participate in dispensing Lazanda have been educated on the risks associated with Lazanda and the requirements of the Lazanda REMS program, as described in the *Pharmacy Education Program*. This training should be documented and is subject to audit.

c) I understand that Lazanda is not bioequivalent with other fentanyl products on a microgram-per-microgram basis and therefore must not be substituted for any other fentanyl products.

d) I understand that Lazanda is contraindicated for use in opioid non-tolerant patients.

e) I understand that the initial starting dose of Lazanda for all patients is the lowest dose (100 mcg).

f) I understand the importance of discussing the risks and benefits of Lazanda with patients and their caregivers, and in particular the importance of taking the drug as prescribed, not sharing with others, and proper disposal.

g) I understand that the Lazanda Medication Guide must be given to the patient or their caregiver each time Lazanda is dispensed.

h) I understand that Lazanda will not be dispensed without verifying through our pharmacy management system that the prescriber and pharmacy are enrolled and active, and that the patient has not been inactivated in the program.

i) I understand that ALL Lazanda prescriptions, regardless of the method of payment, must be processed through our pharmacy management system.

j) I understand that all dispensing locations must be enrolled in the Lazanda REMS program to dispense Lazanda.

k) I understand that Lazanda can only be obtained from wholesalers/distributors that are enrolled in the Lazanda REMS program.

l) I understand that our pharmacy will not sell, loan or transfer Lazanda inventory to any other pharmacy, institution, distributor, or prescriber.

m) I understand that our pharmacy must re-enroll in the Lazanda REMS program and successfully complete the enrollment requirements every two (2) years.

n) I understand that Lazanda is only available through the REMS program. I understand that the pharmacy must comply with the Lazanda REMS program requirements for outpatient pharmacies.

e. ***Inpatient Pharmacies:***

The authorized pharmacist must complete the following requirements to successfully enroll their inpatient pharmacy:

i. Review the Lazanda REMS education program (*Pharmacy Education Program*) and successfully complete the *Pharmacy Knowledge Assessment.*

ii. Complete and sign the *Pharmacy Enrollment Form [Inpatient Pharmacy Enrollment Form]*. In signing the Pharmacy Enrollment Form the authorized pharmacist is required to acknowledge the following:

a) I understand the benefits and risks associated with Lazanda and the requirements of the Lazanda REMS program.

b) I will ensure that our inpatient pharmacists are educated on the risks associated with Lazanda and the requirements of the Lazanda REMS program, as described in the *Pharmacy Education Program*.

c) I understand that Lazanda is not bioequivalent to other fentanyl products on a microgram-per-microgram basis and therefore must not be substituted for other fentanyl products.

d) I understand that Lazanda is contraindicated for use in opioid non-tolerant patients.

e) I understand that the initial starting dose of Lazanda for all patients is the lowest dose (100 mcg).

f) I understand that pharmacies within or associated with the healthcare facility that dispense to outpatients must also be enrolled in and comply with the Lazanda REMS program to dispense Lazanda to outpatients, as described in section B.2.d, above.

g) I understand that our inpatient pharmacy is not to dispense Lazanda for outpatient use.

h) I understand that a prescriber who wants to discharge a patient with an Lazanda prescription, intended to be dispensed by an outpatient pharmacy, will be required to enroll in the REMS program, as described in section B.1 of this REMS.

i) I will establish or oversee the establishment of a system, order sets, protocols and/or other measures to help ensure appropriate patient selection and compliance with the requirements of the Lazanda REMS.

j) I understand that our pharmacy will not sell, loan or transfer Lazanda inventory to any other pharmacy, institution, distributor, or prescriber.

k) I understand that Lazanda can only be obtained from wholesalers/distributors that are enrolled in the Lazanda REMS program.

l) I understand that our pharmacy must re-enroll in the Lazanda REMS program every two (2) years.

m) I understand that Lazanda is available only through the Lazanda REMS program. I understand and agree to comply with the Lazanda REMS program requirements for inpatient pharmacies.

f. Pharmacies (authorized pharmacist) are required to re-enroll every two (2) years.

g. Archimedes will:

i. Ensure that pharmacy enrollment can successfully be completed via the Lazanda REMS website, mail, fax, or by scanning and e-mailing the forms.

ii. Ensure that, as part of the enrollment process, pharmacies receive the following materials that are part of the Lazanda REMS program and are appended:

• *The Lazanda REMS Program Overview (Outpatient Pharmacy, Chain Pharmacy or Inpatient Pharmacy, as applicable)*

• *Medication Guide*

• *Pharmacy Education Program*

• *Pharmacy Enrollment Form (Outpatient, Chain or Inpatient, as applicable)*

• *Pharmacy Knowledge Assessment*

• *Lazanda REMS website*

iii. Ensure that all enrollment forms are complete, and that the authorized pharmacist has successfully completed the knowledge assessment before activating a pharmacy's enrollment in the Lazanda REMS program. For outpatient pharmacies only, Archimedes will also ensure that the upgrades to the pharmacy management system have been validated before enrolling a pharmacy in the Lazanda REMS program.

iv. Ensure that pharmacies are notified when they are successfully enrolled in the Lazanda REMS program, and therefore, certified to dispense Lazanda.

v. Monitor education and enrollment requirements for pharmacies and inactivate non-compliant pharmacies. Upon initial activation of enrollment, pharmacies remain active until a corrective action of inactivation occurs or expiration of the enrollment period.

vi. Ensure that at least 2 weeks prior to first availability of Lazanda to healthcare providers, *Dear Pharmacy Letters* will be sent (one for inpatient pharmacies and one for outpatient pharmacies). The target audience for the letter will include outpatient and inpatient pharmacies that dispense Schedule II drugs and may be involved in dispensing Lazanda. The letter will include information on the risks associated with the use of Lazanda and the requirements of the Lazanda REMS program. The letter will be accompanied by a copy of the Full Prescribing Information (which will include the Medication Guide), and will be available on the Lazanda REMS website for 1 year from the date of the mailing.

The *Dear Pharmacy Letters (Outpatient and Inpatient)* are part of the *Lazanda* REMS Program and are appended.

3. **Lazanda will only be dispensed for outpatient use with evidence or other documentation of safe use conditions**

a. Archimedes will ensure that Lazanda will only be dispensed for outpatient use if there is documentation in the Lazanda REMS system that the dispensing pharmacy, prescriber, and patient are all enrolled and active in the Lazanda REMS program.

b. Patients are passively enrolled in the Lazanda REMS program when their first Lazanda prescription is processed at the pharmacy. This enrollment will be part of the normal prescription processing at the pharmacy and will be captured in the Lazanda REMS system. Prescribers and outpatient pharmacies are enrolled, as previously described in sections B.1 and B.2.a-d, respectively.

c. Prior to dispensing Lazanda, enrolled outpatient pharmacies will electronically verify documentation of the required enrollments by processing the Lazanda prescription through their pharmacy management system.

i. If the required enrollments are verified, a unique authorization code will be issued to allow processing and dispensing of the prescription to the patient.

ii. If one or more of the required enrollments cannot be verified, the Lazanda REMS system will reject the prescription (prior to a claim being forwarded to the payer) and the pharmacy will receive a rejection notice.

d. Following initial activation, patients remain active until a trigger for inactivation occurs. Triggers for patient inactivation include:

i. The patient has not filled a prescription for more than six (6) months.

ii. The patient receives prescriptions for Lazanda from multiple prescribers within an overlapping time frame that is suggestive of misuse, abuse, or addiction.

e. If an active patient transfers from an enrolled prescriber to a non-enrolled or inactive prescriber, the Lazanda REMS program cannot fill the prescription for Lazanda until the new prescriber is active in the Lazanda REMS program.

f. A patient may have more than one current prescriber (e.g., pain management specialist, primary care physician) provided that prescriptions for Lazanda are not for the same or overlapping period of treatment.

g. Documentation and verification of safe use conditions are not required for prescriptions ordered within an inpatient healthcare setting and given to an inpatient.

C. Implementation System

1. Archimedes will ensure that wholesalers/distributors who distribute Lazanda are enrolled in the Lazanda REMS program. The wholesaler/distributor enrollment process is comprised of the following steps that must be completed by the distributor's authorized representative, prior to receiving Lazanda inventory for distribution:

a. Review the distributor Lazanda REMS program materials.

b. Complete and sign the *Distributor Enrollment Form* and send it to the REMS program administrator (by fax, scan and e-mail, or through the Lazanda REMS website). In signing the Distributor Enrollment Form, each distributor is required to indicate they understand that Lazanda is available only through the Lazanda REMS program and that they must comply with program requirements, and acknowledge that:

i. I will ensure that relevant staff are trained on the Lazanda REMS program procedures and will follow the requirements of the Lazanda REMS program.

ii. I will ensure that Lazanda is only distributed to pharmacies whose enrollment has been validated in the Lazanda REMS program.

iii. I will provide data to the Lazanda REMS program including information on shipment to enrolled pharmacies.

iv. I will cooperate with periodic audits or non-compliance investigations to ensure that Lazanda is distributed in accordance with the program requirements.

c. Archimedes will ensure that all forms are complete, prior to enrolling a distributor in the Lazanda REMS program.

d. Archimedes will notify distributors when they are enrolled in the Lazanda REMS program, and therefore, able to distribute Lazanda.

e. Upon initial activation, distributors remain active until an action of inactivation occurs, expiration of the enrollment period, or failure to comply with the pharmacy enrollment verification obligations. If a previously active distributor becomes inactive, the distributor may become active again by completing the distributor enrollment process in its entirety.

f. Distributors will be re-educated and re-enrolled in the Lazanda REMS program every two (2) years.

g. The following distributor materials are part of the Lazanda REMS program and are appended:

• *Dear Distributor Letter*

• *Distributor Enrollment Form*

2. Archimedes will maintain a database of all enrolled entities (prescribers, pharmacies, patients, and distributors) and their status (i.e., active or inactive), and will monitor and evaluate implementation of the Lazanda REMS requirements.

3. Archimedes will develop a REMS system that uses existing pharmacy management systems that allow for the transmission of REMS information using established telecommunication standards. The REMS system should incorporate an open framework that allows a variety of distributors, systems vendors, pharmacies, and prescribers to participate, and that is flexible enough to support the expansion or modification of the REMS requirements, if deemed necessary in the future.

4. Archimedes will monitor distribution data and prescription data to ensure that only actively enrolled distributors are distributing, actively enrolled pharmacies are dispensing, and actively enrolled prescribers for outpatient use are prescribing Lazanda. Additionally, Archimedes will monitor to ensure that Lazanda is only being dispensed for outpatient use to actively enrolled patients of actively enrolled prescribers. Corrective action or inactivation will be instituted by Archimedes if non-compliance is found.

5. Archimedes will monitor prescribers' compliance with the requirement to complete a Patient-Prescriber Agreement with each Lazanda patient, and to submit it to the REMS program within ten (10) business days. This will be accomplished through patient surveys and by reconciling the Patient-Prescriber Agreements submitted to the REMS program with patient enrollment data captured through the pharmacy management system.

6. Archimedes will monitor and evaluate all enrolled outpatient pharmacies, distributors, and the Lazanda REMS program vendors to validate the necessary system upgrades and ensure the program is implemented as directed.

7. Archimedes will evaluate enrolled inpatient pharmacies' compliance with REMS requirements through surveys.

8. Archimedes will maintain a call center to support patients, prescribers, pharmacies, and distributors in interfacing with the Lazanda REMS program.

9. Archimedes will ensure that all materials listed in or appended to the *Lazanda* REMS will be available through the *Lazanda* website www.LazandaREMS.com or by calling the *Lazanda* REMS call center at 1-855-841-4234.

10. Archimedes will notify pharmacies, prescribers, and distributors of forthcoming enrollment expiration and the need to re-enroll in the REMS program. Notifications for patients will be sent to the patient's prescriber.

11. If there are substantive changes to the Lazanda REMS program, Archimedes will update all affected materials and notify pharmacies, prescribers, and distributors of the changes, as applicable. Notifications for patients will be sent to the patient's prescriber. Substantive changes to the Lazanda REMS program are defined as:

    a. Significant changes to the operation of the Lazanda REMS program.

    b. Changes to the Prescribing Information and Medication Guide that affect the risk benefit profile of Lazanda.

12. Based on monitoring and evaluation of the REMS Elements to Assure Safe Use, Archimedes will take reasonable steps to improve implementation of these elements and to maintain compliance with the Lazanda REMS program requirements, as applicable.

III. TIMETABLE FOR SUBMISSION OF ASSESSMENTS

Archimedes will submit REMS Assessments to the FDA every six (6) months for the first year following the approval of the Lazanda 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 days before the submission date of the assessment. Archimedes will submit each assessment so that it will be received by the FDA on or before the due date.

LAZ-2011-001

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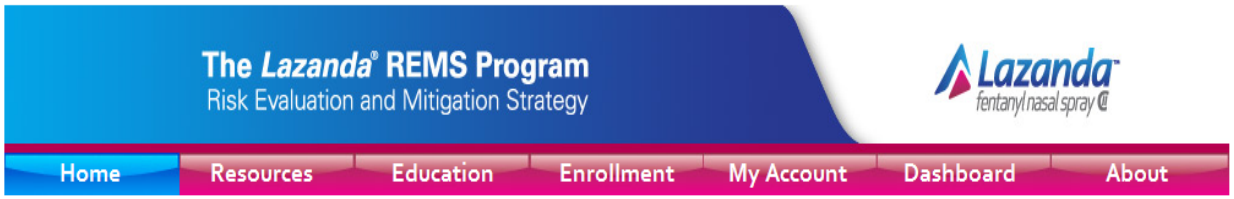
Appendix A: Medication Guide

The Medication Guide is located in Module 1.14.2.2

Appendix B: Lazanda Website Home Page



Log In

Lazanda REMS Program Home

Welcome to the Lazanda REMS Program

The Lazanda REMS Program is the Risk Evaluation and Mitigation Strategy (REMS) for Lazanda (fentanyl) nasal spray.

The goals of the Lazanda REMS program are to mitigate the risk of misuse, abuse, addiction, overdose and serious complications due to medication errors by:

- Prescribing and dispensing Lazanda only to appropriate patients, which includes use only in opioid-tolerant patients.
- Preventing inappropriate conversion between fentanyl products.
- Preventing accidental exposure to children and others from whom it was not prescribed.
- Educating prescribers, pharmacists and patients on the potential of misuse, abuse, addiction and overdose.

To enroll in the Lazanda REMS Program, log in below and follow the directions through the process to become enrolled. For assistance, please call the Lazanda REMS Program at 1-855-841-4234.

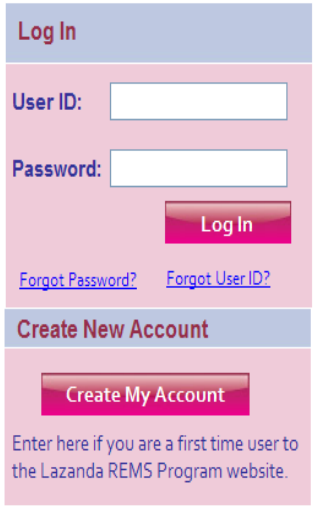
To enroll online:

- Complete the online education
- Submit completed enrollment form.

How to Get Started:

In order to direct you to proper location within the Lazanda REMS website, please Login or create a simple Profile if you are new to the site.

For assistance, please call the Lazanda REMS Program at 1-855-841-4234



Appendix C: Lazanda REMS Education Program

Lazanda® REMS Program

Risk Evaluation and Mitigation Strategy

Education Program

Lazanda® Risk Evaluation and Mitigation Strategy (REMS) Program Goals:

The goals of the Lazanda REMS are to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors by:

1. Prescribing and dispensing Lazanda only to appropriate patients, which includes **use only in opioid-tolerant patients.**
2. Preventing inappropriate conversion between fentanyl products.
3. Preventing accidental exposure to children and others for whom it was not prescribed.
4. Educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose.

Education Program Overview

This Education Program contains key safety information critical for minimizing the risks associated with Lazanda.

The program will address:

- Appropriate patient selection.
- Understanding each patient's risk factors.
- Dosage and administration.
- Patient counseling.
- Effective patient management and follow-up.

Information on the Lazanda REMS program requirements are provided in *An Overview for Prescribers*, *An Overview for Inpatient Pharmacies*, *An Overview for Outpatient Pharmacies*, *An Overview for Chain Pharmacies*, and *An Overview for Patients and Caregivers*, which can be accessed at www.LazandaREMS.com or by calling the Lazanda REMS program at 1-855-841-4234.

This educational program is NOT a substitute for the Prescribing Information.

Please also review the Full Prescribing Information and familiarize yourself with the contents of the Medication Guide.

Appropriate Patient Selection

Indication

Lazanda is indicated only for the management of breakthrough pain in patients with cancer, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for underlying persistent cancer pain.**

Lazanda is contraindicated in opioid non-tolerant patients because life-threatening respiratory depression and death could occur in patients not taking chronic opioids.

Definition of Opioid Tolerance

Patients considered **opioid tolerant** are those who are taking, for 1 week or longer, at least:

- 60 mg oral morphine/day.
- 25 mcg transdermal fentanyl/hour.
- 30 mg oral oxycodone/day.
- 8 mg oral hydromorphone/day.
- 25 mg oral oxymorphone/day.
- OR an equianalgesic dose of another oral opioid.

Lazanda is intended to be **used only in the care of opioid-tolerant patients with cancer** and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Contraindications

- Lazanda **must not** be used in opioid non-tolerant patients, including patients using opioids intermittently, on an as-needed basis.
- Lazanda is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency department.
- Lazanda is contraindicated in patients with known intolerance or hypersensitivity to any of its components or the drug fentanyl.

Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients with other fentanyl products.

Determine Patient-Specific Risk Factors

1. Misuse, Abuse, and Addiction

- Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance. Lazanda can be abused in a manner similar to other opioid agonists, legal and illicit.
- *Consider this abuse liability* when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.
- Risk factors for opioid abuse include:
  - A history of past or current alcohol or drug abuse.
  - A history of psychiatric illness.
  - A family history of illicit drug use.
- Concerns about abuse and addiction should not prevent the proper management of pain.
- All patients treated with opioids require careful monitoring for signs of abuse and addiction because use of opioid analgesic products carries the risk of addiction even under appropriate medical use.
- Proper patient assessment, safe prescribing practices, periodic re- evaluation of therapy, and proper dispensing and storage may help limit the potential for abuse.
- Manage the handling of Lazanda to minimize the risk of abuse, including restriction of access and accounting procedures as appropriate to the clinical setting, and as required by law.

2. Accidental Exposure

- **Lazanda contains a medicine in an amount which can be fatal in:**
  - Children.
  - Individuals for whom it is not prescribed.
  - Those who are not opioid tolerant.
- Lazanda must be kept out of reach of children of all ages, including toddlers through teens, and at all times.
- Prescribers and pharmacists must specifically question patients or caregivers about the presence of children in the home (on a full time or visiting basis).
- Any accidental exposure can be fatal. Talk with your patients and caregivers about safe and appropriate storage of Lazanda.

3. Drug Interactions

- Fentanyl is metabolized mainly via the human cytochrome P450 (CYP3A4) isoenzyme system; therefore potential drug interactions may occur when Lazanda is given concurrently with agents that affect CPY3A4 activity.
- Concomitant use of Lazanda with CYP3A4 inhibitors (eg, certain protease inhibitors, ketoconazole, fluconazole, diltiazem, erythromycin, verapamil) may result in a potentially dangerous increase in fentanyl plasma concentrations, which could increase or prolong the drug effects and may cause potentially fatal respiratory depression.
- Patients receiving Lazanda who begin therapy with, or increase the dose of, CYP3A4

inhibitors are to be carefully monitored for signs of opioid toxicity over an extended period of time. Dosage increases should be done conservatively.

Dosage and Administration

Patients beginning treatment with Lazanda MUST begin with titration from the 100 mcg dose.

Appropriate Conversion

- Lazanda is not equivalent to any other fentanyl product on a microgram-per-microgram basis.
  - **Do NOT convert patients on a mcg per mcg basis from any other fentanyl product to Lazanda.** All patients must begin Lazanda treatment using one 100 mcg dose of Lazanda.
  - **Do NOT substitute Lazanda for any other fentanyl product.**
- Substantial differences exist in the pharmacokinetic profile of Lazanda compared to other fentanyl products that result in clinically important differences in the rate and extent of absorption of fentanyl.
- **As a result of these differences, the substitution of Lazanda for any other fentanyl product may result in fatal overdose.**

Titration

The titration steps are as follows:

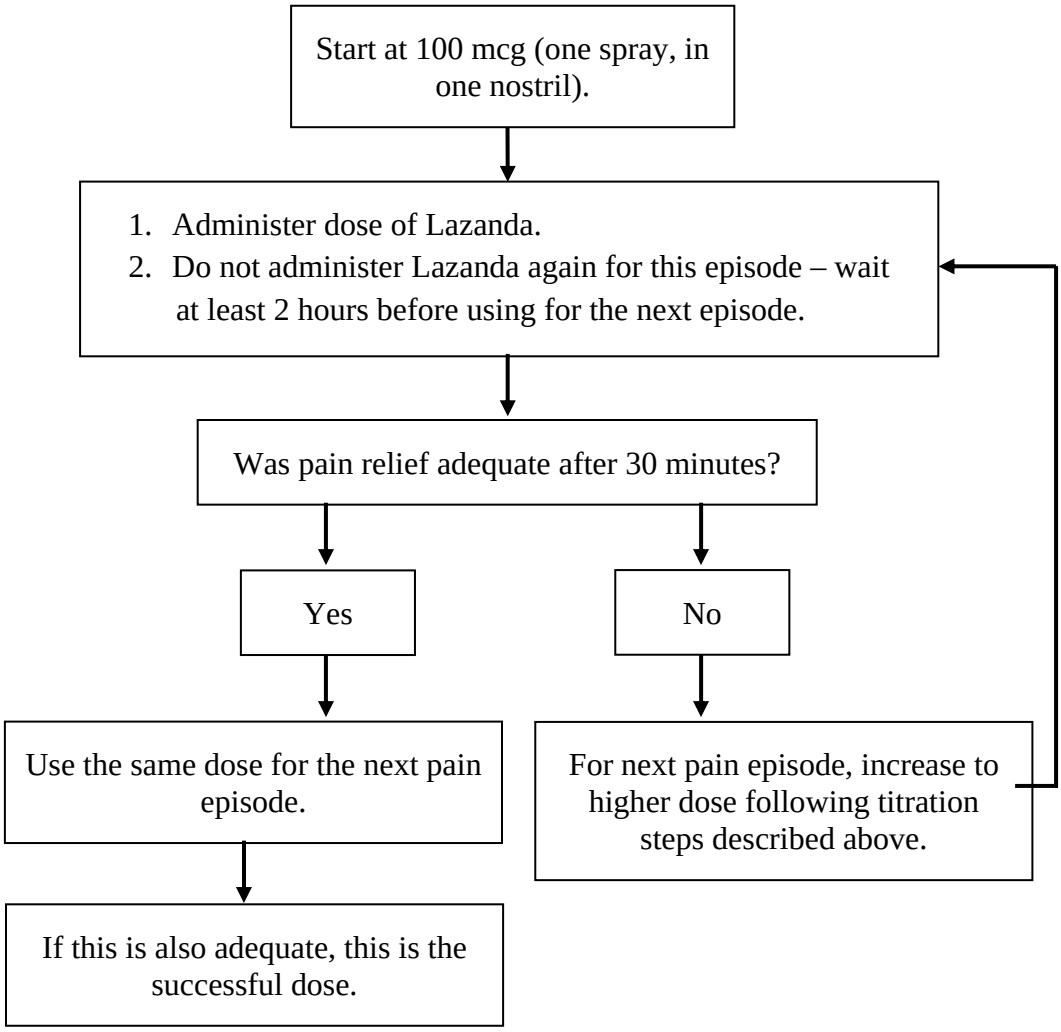
- Lazanda Dose	- Using
- **100 mcg**	- **1 x 100 mcg spray**
- **200 mcg**	- **2 x 100 mcg spray (1 in each nostril)**
- **400 mcg**	- **1 x 400 mcg spray**
- **800 mcg**	- **2 x 400 mcg spray (1 in each nostril)**

Patients should confirm the dose of Lazanda that works for them with a second episode of breakthrough pain and review their experience with their physicians to determine if that dose is appropriate, or whether a further adjustment is warranted.

The safety and efficacy of doses higher than 800 mcg have not been evaluated in clinical studies. There are no clinical data to support the use of a combination of dose strengths to treat an episode.

Individually titrate Lazanda to a dose that provides adequate analgesia with tolerable side effects.

- **Only use Lazanda once per breakthrough pain cancer episode;** i.e. do not redose Lazanda within an episode.
- **Single doses should be separated by at least 2 hours.**



Maintenance/Dose Adjustments

- Once a successful dose is found, that dose should be prescribed for each subsequent breakthrough cancer pain episode.
- Limit Lazanda use to 4 or fewer doses per day.
- If the prescribed dose no longer adequately manages the cancer breakthrough pain for several consecutive episodes, increase the dose as described in the Titration section.
- Consider increasing the dose of the around-the-clock opioid medicine used for persistent cancer pain in patients experiencing more than 4 breakthrough cancer pain episodes per day.

Administration

- The patient should be instructed to prime the device before use by spraying into the pouch (4 sprays in total), until a green bar or a number appears in the counting window, following the instructions for use in the Medication Guide.
- Instruct the patient to insert the nozzle of the Lazanda bottle a short distance (about ½

inch or 1 cm) into their nose and point towards the bridge of the nose, titling the bottle slightly. The patient should press down firmly on the finger grips until they hear a "click" and the number in the counting window advances by one.
- Advise patients that the fine mist spray is not always felt on the nasal mucosal membrane and to rely on the audible click and the advancement of the dose counter to confirm a spray has been administered.

A video showing how to use Lazanda is available on-line at www.LazandaREMS.com or on DVD by calling 1-855-841-4234.

Disposal

- Patients and caregivers must be instructed to properly dispose of all unused, partially used, and used Lazanda bottles.
- The remaining liquid in all bottles must be sprayed into the pouch, provided in the pack, for safe disposal as soon as possible.
- If there are any unwanted therapeutic sprays remaining in the bottle, instruct the patient to spray these into the pouch until the number "8" appears in the counting window and there are no more full therapeutic sprays obtainable from the bottle.
- After the counter has advanced to "8", the patient should continue to push down on the finger grips a total of 4 times in order to expel any residual medicine from the bottle.
- After the 8 therapeutic sprays have been emitted, the patient will not hear a click and the counter will not advance beyond "8"; further sprays emitted will not be full sprays and should always be trapped in the pouch, **not** used therapeutically.
- **The patient and caregiver must be instructed to seal the pouch and place both it and the empty bottle into the child-resistant storage container**.
- Hands must be washed with soap and water immediately after handling the pouch.
- The patient must discard the child-resistant container containing the pouch and the bottle in the trash.
- The patient or caregiver must continue to store the Lazanda bottle in the specially provided child-resistant container and the pouch out of the reach of children until proper disposal, as described above, is possible.

Instruct the patient to dispose of the Lazanda bottle and start a new one if:

- It has been 5 days or more since they last used the bottle of Lazanda
- It has been 14 days or more since they primed the bottle.

Patient Counseling

Before initiating treatment with Lazanda, review the Medication Guide with patients and caregivers, and counsel them on Lazanda risks and safe use.

- Review how much the patient can take, and how often.

Tell the patient:

- You must be regularly using another opioid pain medicine, around-the-clock, for your constant pain.
- If you stop taking your around-the-clock opioid pain medicine for your constant pain, you must stop taking Lazanda.
- Lazanda can cause serious side effects, including life-threatening breathing problems which can lead to death. You must take Lazanda exactly as prescribed. Always wait at least 2 hours before treating another episode of breakthrough cancer pain.
- Contact me or my office if Lazanda does not relieve your pain. Do not change your dose of Lazanda or take Lazanda more often than I have directed.
- Always store Lazanda in a safe place away from children and teenagers because accidental use by a child, or anyone for whom it was not prescribed, is a medical emergency and can cause death.
- Properly dispose of unused and remaining Lazanda. Do so as soon as you no longer need it. Empty the bottle by spraying unused Lazanda repeatedly into the special pouch provided. Seal the pouch and put it into the child-resistant container with the empty bottle. Throw the child-resistant container with the empty bottle and sealed pouch into the trash.
- Never give Lazanda to anyone else, even if they have the same symptoms, since it may harm them or even cause death.
- Never sell or give away Lazanda. Doing so is against the law.

Effective Patient Management and Follow-up

All patients treated with opioids require careful monitoring. At follow-up visits:

- Assess appropriateness of dosage, and make any necessary dose adjustments to Lazanda or to their around-the-clock opioid medication.
- Assess for signs of misuse, abuse, or addiction.
- Be aware that abuse and addiction are separate and distinct from physical dependence and tolerance.
  - Abuse of opioids can occur in the absence of addiction, and is characterized by misuse for nonmedical purposes, often in combination with other psychoactive substances.

- The possibility of physical and/or psychological dependence should be considered when a pattern of inappropriate behavior is observed.

- Careful record keeping of prescribing information, including quantity, frequency, and renewal requests, is strongly advised.

Appendix D: Lazanda Knowledge Assessment

1 KNOWLEDGE ASSESSMENT

You're now going to review 10 clinical settings that will test your knowledge of appropriate use and prescribing of Lazanda®.

Once completed, please fill in your details on both pages, tear out the pages, and fax to the Lazanda REMS program at 1-855-841-4235. If taken on the Lazanda website, your test/answers will be kept there.

Prescriber Information

Name:	
Identifier:	
NPI Number:	DEA Number:
State License Number:	License State:

Outpatient Pharmacy Information

Authorized Pharmacist* Name:	*or Authorized Chain Pharmacy Representative
DEA Number or Chain ID:	
NPI Number:	NCPDP:
Medicaid ID:	ZIP:

Inpatient Pharmacy Information

Authorized Pharmacist* Name:	
DEA Number:	ZIP:

QUESTION 1

The patients described below are all experiencing breakthrough pain, but one is not an appropriate patient for Lazanda. Which patient should not receive Lazanda? *Select <u>one</u> option*.

- ☐ 1. Adult male with advanced lung cancer, on 60 mg of oral morphine daily for the past 4 weeks.
- ☐ 2. Adult female with advanced breast cancer, her underlying persistent cancer pain is managed with 25 mcg/hour transdermal fentanyl patches for the past 2 months.
- ☐ 3. Adult female with multiple myeloma, which returned after remission, who has bone pain managed with 50 mg oral oxymorphone daily for the last 2 weeks.
- ☐ 4. 16-year-old sarcoma patient, using transdermal fentanyl for his underlying persistent cancer pain.

QUESTION 2

Patients described below are experiencing breakthrough pain. Lazanda is not appropriate for one of them. Which patient should not receive Lazanda? *Select <u>one</u> option.*

- ☐ 1. Adult female with breast cancer, who just completed a mastectomy and reconstructive surgery and who experiences persistent cancer pain, managed with 45 mg oral morphine a day for the past 6 weeks.
- ☐ 2. Adult female with advanced cervical cancer, who has been taking a daily dose of 12 mg oral hydromorphone for the past 3 weeks.
- ☐ 3. Adult male with advanced prostate cancer, who has been taking 100 mg oral morphine daily for pain secondary to sacral metastases for 2 weeks.
- ☐ 4. Adult female with advanced lung cancer and underlying persistent cancer pain, managed with 25 mcg/hour transdermal fentanyl patches for 8 weeks.

Authorized Pharmacist (insert check box) /Prescriber Name (insert check box):	DEA Number:

QUESTION 3

A patient is taking another transmucosal fentanyl product (ie, Fentora, Onsolis, or Actiq), but wants to change his medication. His doctor decides to prescribe Lazanda®. How should the prescriber proceed? *Select <u>one</u> option*.

- ☐ 1. Switch from the other transmucosal fentanyl product to Lazanda at half the dose.
- ☐ 2. The prescriber can safely substitute the equivalent dosage of Lazanda as it has the same effect as other transmucosal fentanyl products.
- ☐ 3. The prescriber should base the starting dose of Lazanda on the dose of opioid medication used for underlying persistent cancer pain.
- ☐ 4. The prescriber must not substitute the equivalent Lazanda dose for other transmucosal fentanyl products because they have different absorption properties and this could result in fentanyl overdose.

QUESTION 4

A patient is starting titration with Lazanda. What dose must they start with? *Select <u>one</u> option.*

- ☐ 1. 100 mcg.
- ☐ 2. 200 mcg.
- ☐ 3. 400 mcg.
- ☐ 4. 800 mcg.

QUESTION 5

Certain factors may increase the risk of abuse and/or diversion of opiate medications. Which of the following is most accurate? *Select <u>one</u> option.*

- ☐ 1. The patient has a household member with a street drug abuse problem.
- ☐ 2. The patient has a history of prescription drug misuse.
- ☐ 3. The patient or a close family member has a history of alcohol abuse.
- ☐ 4. All of the above.

QUESTION 6

A patient is taking Lazanda and their doctor would like to prescribe ketoconazole, a CYP3A4 inhibitor. Which of the following statements is true? *Select <u>one</u> option.*

- ☐ 1. There is no possible drug interaction between CYP3A4 inhibitors and Lazanda.
- ☐ 2. Use of Lazanda with a CYP3A4 inhibitor may require dosage adjustment; carefully monitor the patient for opioid toxicity, otherwise such use may cause potentially fatal respiratory depression.
- ☐ 3. The dose of Lazanda must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.
- ☐ 4. The patient can't be prescribed ketoconazole, because using it at the same time as the other drug could be fatal.

Authorized Pharmacist (insert check box) /Prescriber Name (insert check box)	DEA Number:

QUESTION 7

A prescriber has begun titrating a patient with 100 mcg of Lazanda®. However, after 30 minutes, the breakthrough pain has not been sufficiently relieved. What should he advise the patient to do? *Select <u>one</u> option.*

- ☐ 1. Wait 10 minutes (ie, total of 40 minutes since initial Lazanda dose), then if pain is still present, take another 100 mcg.
- ☐ 2. Take another dose of 100 mcg immediately.
- ☐ 3. Wait until the next episode of pain occurs, and if that is at least 2 hours later, take a 200 mcg dose (2 sprays of 100 mcg).
- ☐ 4. Double the dose to 200 mcg and take immediately.

QUESTION 8

There is a risk of fatal overdose with inappropriate use of Lazanda. Which one of the following answers is most accurate? *Select <u>one</u> option.*

100
- ☐ 1. Lazanda can be fatal if taken by anyone for whom it is not prescribed.
- 2. Lazanda can be fatal if taken by children.
- ☐ 3. Lazanda can be fatal if taken by anyone who is not opioid tolerant.
- 4. All of the above.

☐

QUESTION 9

The Lazanda Medication Guide contains important information for the patient and their caregiver. Which one of the following statements is most accurate? *Select <u>one</u> option.*

- ☐ 1. It is the pharmacist's responsibility alone to counsel the patient to read the Lazanda Medication Guide.
- ☐ 2. The patient must be counseled to read the Medication Guide only on the first Lazanda prescription.
- ☐ 3. The Lazanda REMS program will provide a Medication Guide by mail to the patient after Lazanda is dispensed.
- ☐ 4. The patient must be counseled to read the Lazanda Medication Guide with every prescription because important information may have changed.

QUESTION 10

Which one of the following statements is most accurate regarding the safe storage and disposal of Lazanda? *Select <u>one</u> option.*

- ☐ 1. Lazanda should be protected from theft.
- ☐ 2. Lazanda should be kept in a safe place and out of the reach of children.
- ☐ 3. Dispose of unused medication by squirting it into the carbon pouch until the bottle is empty.
- ☐ 4. All of the above.

Authorized Pharmacist (insert check box) Prescriber Name (insert check box)	DEA Number:

Appendix E: Prescriber Enrollment Form

[Logo]

The Lazanda® REMS Program Prescriber Enrollment Form

To enroll in the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program, please complete the form below. When complete, please fax the form, along with the Prescriber Knowledge Assessment, to the Lazanda REMS program at 1-855-841-4235.

First Name:	**Middle Name:**	**Last Name:**	**Suffix (Degree):**	
Site Name*:				
Address:		**City:**	**State:**	**ZIP:**
State License Number*:		**License State:**		
NPI Number:		**DEA Number*:**		
Office Phone Number:		**Fax Number:**		
E-mail Address:				
Preferred Channel of Communication: E-mail …☐ Fax…☐				

I understand that Lazanda (fentanyl) spray is only available through the Lazanda REMS program and I must comply with the program requirements. In addition, I acknowledge that:

1) I have reviewed the Lazanda Full Prescribing Information and the Education Program and I have completed the Prescriber Knowledge Assessment. I understand the responsible use conditions for Lazanda and the risks and benefits of chronic opioid therapy.
2) I understand that Lazanda can be abused and that this risk should be considered when prescribing or dispensing Lazanda in situations where I am concerned about an increased risk of misuse, abuse, or overdose, whether accidental or intentional.
3) I understand that Lazanda is indicated only for the management of breakthrough pain in patients with cancer, who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.
4) I understand that Lazanda is contraindicated for use in opioid non-tolerant patients, and know that fatal overdose can occur at any dose.
5) I understand that Lazanda must not be used to treat any contraindicated conditions such as acute or postoperative pain, including headache/migraine.
6) I understand that the initial starting dose of Lazanda for <u>all</u> patients is the lowest dose (100 mcg), and that patients must be titrated individually.
7) I understand that Lazanda is not bioequivalent with any other fentanyl product (regardless of route of administration), and that substitution may result in fatal overdose. I understand that patients switching from another fentanyl product to Lazanda must not be converted on a microgram-per-microgram basis.
8) I will complete and sign a Lazanda REMS Patient-Prescriber Agreement with <u>each</u> new patient, before writing the patient's first prescription, and re-new the agreement every 2 years.
9) I will provide a completed signed copy of the Patient-Prescriber Agreement to the patient and retain a copy for my records. I will also provide a completed signed copy to the Lazanda REMS program (by fax or through the Lazanda REMS website) within 10 working days.
10) At follow-up visits, I agree to assess the patient for appropriateness of the dose, and for signs of misuse and abuse.
11) I understand that Lazanda is only available through the Lazanda REMS program. I understand and agree to comply with the Lazanda REMS program requirements for prescribers.

Signature:_____ **Date:**_____

* If you have additional sites, or state license or DEA numbers, that you may use when prescribing Lazanda, please complete overleaf.

Additional Prescriber Information

Site Name*:			
Address:	**City:**	**State:**	**ZIP:**
Office Phone Number:	**Fax Number:**		

Site Name*:			
Address:	**City:**	**State:**	**ZIP:**
Office Phone Number:	**Fax Number:**		

Site Name*:			
Address:	**City:**	**State:**	**ZIP:**
Office Phone Number:	**Fax Number:**		

DEA Number*:_____

DEA Number*:_____

DEA Number*:_____

State License Number*:	**License State:**

State License Number*:	**License State:**

State License Number*:	**License State:**

If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

This form is part of an FDA-approved REMS.

Appendix F: Patient-Prescriber Agreement

[Logo] **Lazanda® (fentanyl) nasal spray**

The Lazanda® REMS Program Patient-Prescriber Agreement

When complete, please fax the form to the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program at 1-855-841-4235.
IMPORTANT: We highly encourage online completion and submission, as this will facilitate faster administrative processing.

As the prescriber of Lazanda, I acknowledge that:

1. Patient is currently using around-the-clock opioid analgesia and has been for at least 1 week.
2. Patient is opioid tolerant. Patients considered opioid tolerant are those who are regularly taking at least: 60 mg oral morphine/day; 25 mcg transdermal fentanyl/hour; 30 mg oral oxycodone/day; 8 mg oral hydromorphone/day; 25 mg oral oxymorphone/day; or an equianalgesic dose of another opioid for 1 week or longer.
3. The Lazanda Medication Guide has been provided to and reviewed with the patient or their caregiver.
4. The patient or their caregiver has been counseled about the risks, benefits, and appropriate use of Lazanda, including communication of the following safety messages:
   a) If patients stop taking their around-the-clock opioid medication, they must stop taking Lazanda.
   b) NEVER share Lazanda.
   c) Giving Lazanda to someone for whom it has not been prescribed can result in a fatal overdose.
   d) Lazanda can be fatal to a child; used and unused dosage units must be safely stored out of the reach of children living in or likely to visit the home.

Prescriber
Signature: _____ **First Name:** _____ **Last Name:** _____

Suffix (Degree):_____ **DEA Number:** _____

Fax Number:_____ **Date:**_____ **NPI #:** _____

As the patient being prescribed Lazanda, or a legally authorized representative, I acknowledge that:

1) My prescriber has given me a copy of the Lazanda Medication Guide and has reviewed it with me.
2) I understand that before I can take Lazanda, I must be regularly using another opioid pain medicine, around-the-clock, for my constant pain.
3) I understand that if I stop taking my around-the-clock opioid pain medicine for my constant pain, I must stop taking Lazanda.
4) I understand how I should take Lazanda, including how much I can take, and how often I can take it.
5) I understand that Lazanda can cause serious side effects, including life-threatening breathing problems which can lead to death, especially if I do not take Lazanda exactly as my prescriber has directed me to take it.
6) I agree to contact my prescriber if Lazanda does not relieve my pain. I will not change my dose of Lazanda myself or take Lazanda more often than my prescriber has directed.
7) I agree that I will never give Lazanda to anyone else, even if they have the same symptoms, since it may harm them or even cause death.
8) I will store Lazanda in a safe place away from children and teenagers because accidental use by a child, or anyone for whom it was not prescribed, is a medical emergency and can cause death.
9) I have been instructed on how to properly dispose of unused and remaining Lazanda and will dispose of Lazanda as soon as I no longer need it.
10) I understand that selling or giving away Lazanda is against the law.
11) I have asked my prescriber all the questions I have about Lazanda. If I have any additional questions or concerns in the future about my treatment with Lazanda, I will contact my prescriber.
12) I have reviewed the Patient Authorization for Disclosure and Use of Health Information for Lazanda REMS and authorize my healthcare providers and health plans to disclose my personal and medical information to Archimedes Pharma US Inc., (the maker of Lazanda) and its agents and contractors as necessary to administer the Lazanda REMS program. My personal health information will not be otherwise disclosed except (1) as required by law or (2) in certain circumstances as necessary to protect public health.

Logo: For more information about Lazanda®, please see Full Prescribing Information, including BOXED WARNINGS LAZ-xxxx

Patient:

Patient Signature: _____ Date: _____

First Name:_____ Middle Initial:____ Last Name:_____ ZIP:_____

Date of Birth (MM/DD/YYYY):_____ Phone Number:_____ State:_____

Patient Representative (if required)

Signature:_____ Relationship to Patient:_____

First Name:_____ Last Name:_____ Date:_____

Phone Number:_____ State:_____

Patient Authorization for Disclosure and Use of Health Information for Lazanda REMS Program

I hereby authorize each of my physicians, pharmacists, and other healthcare providers (together, "Providers") and each of my health insurers (together, "Insurers") to disclose personally identifiable health information, including information related to my medical diagnosis, condition, and treatment (including lab and prescription information), and my name, address, and telephone number (together, "Health Information") to Archimedes Pharma US Inc., its agents and representatives, including authorized third parties, as necessary to administer the Lazanda REMS program (together, "Archimedes") for the purposes described below.

Specifically, I authorize Archimedes to receive, use, and disclose my Health Information in order to:

I. Enroll me in the Lazanda REMS program and administer my participation (including contacting me) in the Lazanda REMS program.
II. Evaluate the appropriate use of Lazanda and the effectiveness of the Lazanda REMS program.
III. Provide me with educational information with respect to the Lazanda REMS program.
IV. Contact my Providers to collect, enter, and maintain my Health Information in a secure Lazanda REMS database.
V. Make submissions to the FDA, regarding matters such as adverse events and Lazanda REMS program effectiveness.

While I understand I am not required to sign this Authorization, if I do not do so, then I will not be able to enroll in the Lazanda REMS program and will not be able to receive Lazanda.

I understand that I may revoke (withdraw) this Authorization at any time by faxing a signed, written request to the Lazanda REMS program at 1-855-841-4235. Archimedes shall notify my Providers and Insurers of my revocation, who may no longer disclose my Health Information to Archimedes once they have received and processed that notice. Revoking this Authorization will not affect Archimedes' ability to use and disclose my Health Information that it has already received to the extent permitted under applicable law. If I revoke this Authorization, I will no longer be able to participate in the Lazanda REMS program to receive Lazanda.

Archimedes agrees to protect my information by using and disclosing it only for the purposes described.

Logo: For more information about Lazanda®, please see Full Prescribing Information, including BOXED WARNINGS LAZ-xxxx

If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

This form is part of an FDA-approved REMS.

Appendix G: Lazanda REMS: An Overview for Prescribers

The Lazanda® REMS Program - An Overview for Prescribers

What Is Lazanda®?

Lazanda is a fentanyl nasal spray indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain**.

What Is the Lazanda REMS Program?

The Lazanda Risk Evaluation and Mitigation Strategy (REMS) program is designed to ensure informed risk-benefit decisions before initiating treatment, and while patients are on treatment, to ensure appropriate use of Lazanda (fentanyl) nasal spray. Because of the risk for misuse, abuse, addiction, and overdose, Lazanda is available only through a program required by the Food and Drug Administration, called the Lazanda REMS program.

Outpatient Setting

In an outpatient setting, only prescribers, pharmacies, distributors, and patients enrolled in the program are able to prescribe, dispense, distribute, and receive Lazanda, respectively, under the Lazanda REMS program.

Inpatient Setting

For inpatient administration of Lazanda, patient and prescriber enrollment in the Lazanda REMS program is not required. Only the inpatient pharmacy is required to be enrolled to order and dispense Lazanda for inpatient use. Inpatient pharmacies may not dispense Lazanda for outpatient use.

How to Enroll in the Lazanda REMS Program

In order to reduce the risks of inappropriate patient selection and ensure appropriate dosing and administration of Lazanda, you will be enrolled only after successful completion of a knowledge assessment (Prescriber Knowledge Assessment). Educational opportunities and knowledge assessment questions are available online at www.LazandaREMS.com or by contacting the Lazanda REMS call center at 1-855-841-4234 to request materials. You will also be required to attest to your understanding of the appropriate use of Lazanda and adherence to the Lazanda REMS program.

Without this enrollment, you will not be eligible to prescribe Lazanda for outpatient use. In addition, only enrolled pharmacies are eligible to dispense Lazanda prescriptions. Outpatient prescriptions written by unenrolled prescribers, or for unenrolled patients, will not be authorized by the Lazanda REMS program and will not be dispensed to the patient.

Prescribers and pharmacies are required to acknowledge their understanding of the potential risks involved with the inappropriate use of Lazanda. Prescribers and pharmacies should ensure:

- Completion of the relevant education program and knowledge assessment, and submission of the relevant enrollment forms to the Lazanda REMS program.
- Appropriate patient selection.

- Completion and submission of a patient-prescriber agreement to the Lazanda REMS program (not required for inpatients).
- That patients are provided with relevant Lazanda REMS program materials and educated on the benefits and risks of treatment with Lazanda.

Overview of Steps for the Lazanda REMS Program

Step 1. Prescriber Education and Enrollment (Outpatient Prescribing)

- Initiate the enrollment process by selecting the appropriate button on the Home page at www.LazandaREMS.com.
- Enter your demographic information.
- Set up your user name and password.
- Review the Lazanda REMS prescriber educational materials, including the Full Prescribing Information, and successfully complete the Prescriber Knowledge Assessment.
- Complete and submit the Prescriber Enrollment Form (including attestations) and renew that agreement every 2 years.

Step 2. Patient Education

- Identify appropriate patients.
- Counsel the patient about the benefits and risks of Lazanda and together review the Medication Guide.
- Encourage the patient to ask questions.
- Complete the Patient-Prescriber Agreement, which must be printed off and then signed by both you and your patient (not required for inpatients).
- Submit the signed Patient-Prescriber Agreement to the Lazanda REMS program via fax to 1-855-841-4235 or through the Lazanda REMS website at www.LazandaREMS.com
- We encourage you to submit this agreement immediately, if possible; it must, however, be submitted within 10 business days of completing the agreement. **The next prescription for Lazanda will not be authorized for dispensing if this form has not been received by the Lazanda REMS program.**

Step 3. Prescribing

- Write prescription for Lazanda.
- Help each patient to find pharmacies which are certified in the Lazanda REMS program. A list of Lazanda REMS–certified pharmacies can be found at www.LazandaREMS.com or by calling 1-855-841-4234.

Step 4. Monitoring

- Promptly report suspected adverse events, including misuse, abuse, and overdose directly to Archimedes Pharma by calling 1-866-435-6775.
- Respond to requests for additional information from the Lazanda REMS program.

Further Information

For more information on the REMS program, you can call the Lazanda REMS program at 1-855-841-4234 or visit www.LazandaREMS.com.

Important Safety Information

Boxed Warnings

[BEGIN BOX]

WARNINGS: POTENTIAL FOR ABUSE and IMPORTANCE OF PROPER PATIENT SELECTION

Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. Lazanda can be abused in a manner similar to other opioid agonists. Consider the potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion. Schedule II opioid substances which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with other transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients) and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

Lazanda is indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine/daily, or at least 25 mcg transdermal fentanyl/hour, or at least 30 mg of oral oxycodone daily, or at least 8 mg oral hydromorphone daily, at least 25 mg oral oxymorphone daily or an equianalgesic dose of another opioid for a week or longer.

Lazanda is contraindicated in opioid non-tolerant patients and is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl product to Lazanda. Patients beginning treatment with Lazanda must begin with titration from the 100 mcg dose.

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics profile of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda®. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda.

Lazanda is intended to be used only in the care of opioid tolerant patients with cancer and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda contains a medicine in an amount that can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times.

The concomitant use of Lazanda with cytochrome P450 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

[END BOX]

Adverse Reactions
The most commonly observed adverse events seen with Lazanda are typical of opioid side effects, such as nausea, constipation, somnolence, and headache. Expect opioid side effects and manage them accordingly.

Further Information
If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

www.LazandaREMS.com
Lazanda® is a trademark of Archimedes Development Ltd.

Appendix H: Lazanda REMS DHCP Letter

The Lazanda® REMS Program – Dear Healthcare Provider Letter

Important Drug Warning
Subject: Risk of misuse, abuse, addiction, and overdose for Lazanda® (fentanyl) nasal spray; FDA-required restricted-distribution program

Dear Healthcare Provider:

Archimedes Pharma would like to inform you of the approval of Lazanda (fentanyl) nasal spray, a treatment for breakthrough pain (BTPc) in opioid-tolerant cancer patients. Because of the potential risk of misuse, abuse, addiction, and overdose, Lazanda is only available through the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program. In an outpatient setting, only prescribers, pharmacies, distributors, and patients enrolled in the program are able to prescribe, dispense, distribute, and receive Lazanda, respectively, under the Lazanda REMS program.

Lazanda is an opioid analgesic indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain**.

Patients considered opioid tolerant are those who are taking at least: 60 mg oral morphine/day; 25 mcg transdermal fentanyl/hour; 30 mg oral oxycodone/day; 8 mg oral hydromorphone/day; 25 mg oral oxymorphone/day; or an equianalgesic dose of another opioid for 1 week or longer.

Inpatient Setting

For inpatient administration of Lazanda, patient and prescriber enrollment in the Lazanda REMS program are not required. Inpatient pharmacy enrollment is required.

Outpatient Setting

To prescribe Lazanda in an outpatient setting, you need to register in the Lazanda REMS program, and you must:

- Review the Education Program and the Lazanda Full Prescribing Information.
- Successfully complete the Prescriber Knowledge Assessment.
- Complete the Prescriber Enrollment Form.
- Complete and sign a Patient-Prescriber Agreement with each new patient.
- Re-enroll every 2 years.

To enroll in the Lazanda REMS program, visit www.LazandaREMS.com or call 1-855-841-4234.

Lazanda REMS
The goals of the Lazanda REMS are to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors by:

1. Prescribing and dispensing Lazanda only to appropriate patients, which includes **use only in opioid-tolerant patients**.
2. Preventing inappropriate conversion between fentanyl products.
3. Preventing accidental exposure to children and others for whom it was not prescribed.
4. Educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose.

Important Safety Information

Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. Lazanda can be abused in a manner similar to other opioid agonists. Consider the potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion. Schedule II opioid substances, which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with other oral transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (eg, use in opioid non-tolerant patients) and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

Lazanda is contraindicated in opioid non-tolerant patients and is contraindicated in the management of acute or postoperative pain, including headache/migraine or dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl product to Lazanda. Patients starting treatment with Lazanda must begin titration with the 100 mcg dose.

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda.

Lazanda is intended to be **used only in the care of opioid-tolerant patients with cancer** and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda contains a medicine in an amount that can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times.

The concomitant use of Lazanda with cytochrome P450 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

Adverse Reactions
The most commonly observed adverse events seen with Lazanda are typical of opioid side effects, such as nausea, constipation, somnolence, and headache. Expect opioid side effects and manage them accordingly

Medication Guide
It is important that you discuss the risks of Lazanda with your patients and encourage them to read the Medication Guide (included in the attached Full Prescribing Information). The Medication Guide provides important information on the safe and effective use of Lazanda and will be provided to patients with each prescription. Patients should be counseled on the need to store Lazanda safely out of the reach of children and household acquaintances.

Adverse Event Reporting
Prescribers should report all adverse events associated with the use of Lazanda directly to Archimedes Pharma at 1-866-435-6775.

Please see the attached Full Prescribing Information, including boxed warnings, and Medication Guide for important safety information for Lazanda.

Further Information
If you have questions about the Lazanda REMS program, please visit www.LazandaREMS.com for more information or call the toll-free number, 1-855-841-4234.

Thank you,

Linda Wase, MD
Senior Vice President &Chief Medical Officer, Archimedes Pharma

This letter is part of an FDA-approved REMS.

Appendix I: Lazanda REMS Outpatient Pharmacy Enrollment Forms

[Logo] **Lazanda® (fentanyl) nasal spray**

The Lazanda® REMS Program Outpatient Pharmacy Enrollment Form

The authorized responsible site pharmacist must complete the form below. When complete, please fax the form, along with the completed Pharmacy Knowledge Assessment, to the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program at 1-855-841-4235. If you are a chain pharmacy, please complete the Chain Pharmacy Enrollment Form, which can be found at www.LazandaREMS.com or at 1-855-841-4234.

I understand that Lazanda (fentanyl nasal spray) is only available through the Lazanda REMS program and I must comply with the program requirements. In addition, as the designated authorized pharmacist, I acknowledge that:

1) I have reviewed the Lazanda Full Prescribing Information and the Education Program and I have completed the Pharmacy Knowledge Assessment. I understand the risks and benefits associated with Lazanda and the requirements of the Lazanda REMS program for pharmacies.
2) I will ensure that all pharmacy staff who participate in dispensing Lazanda have been educated on the risks associated with Lazanda and the requirements of the Lazanda REMS program, as described in the Education Program. This training should be documented and is subject to audit.
3) I understand that Lazanda is not bioequivalent with other fentanyl products on a microgram-per-microgram basis and therefore must not be substituted for any other fentanyl products.
4) I understand that Lazanda is contraindicated for use in opioid non-tolerant patients.
5) I understand that the initial starting dose of Lazanda for all patients is the lowest dose (100 mcg).
6) I understand the importance of discussing the risks and benefits of Lazanda with patients and their caregivers, and in particular the importance of taking the drug as prescribed, not sharing with others, and proper disposal.
7) I understand that the Lazanda Medication Guide must be given to the patient or their caregiver each time Lazanda is dispensed.
8) I understand that Lazanda will not be dispensed without verifying through our pharmacy management system that the prescriber and pharmacy are enrolled and active, and that the patient has not been inactivated in the program.
9) I understand that ALL Lazanda prescriptions, regardless of the method of payment, must be processed through our pharmacy management system.
10) I understand that all dispensing locations must be enrolled in the Lazanda REMS program to dispense Lazanda.
11) I understand that Lazanda can only be obtained from wholesalers/distributors that are enrolled in the Lazanda REMS program.
12) I understand that our pharmacy will not sell, loan, or transfer Lazanda inventory to any other pharmacy, institution, distributor, or prescriber.
13) I understand that our pharmacy must re-enroll in the Lazanda REMS program and successfully complete the enrollment requirements every 2 years.
14) I understand that Lazanda is only available through the REMS program. I understand that the pharmacy must comply with the Lazanda REMS program requirements for outpatient pharmacies.

Authorized Pharmacist Signature: _____
Date:_____
Title:_____
First Name:_____ Last Name:_____

Pharmacy Information

Pharmacy Name:			
Address:	**City:**	**State:**	**ZIP:**
Medicaid ID:		**State Issued:**	
Fax Number:	**Phone Number:**		
NPI Number:	**DEA Number:**		
E-mail Address:	**NCPDP Number:**		
Preferred Channel of Communication: E-mail …☐ Fax…☐			

Preferred e-mail for program communications (Please tick one):

▢ Authorized pharmacist e-mail address ▢ Pharmacy e-mail address

Medicaid ID:_____ State Issued:_____
Medicaid ID:_____ State Issued:_____
Medicaid ID:_____ State Issued:_____

Please fax the completed form to the Lazanda REMS program at 1-855-841-4235.
You will receive a fax or e-mail with instructions of how to submit test transaction(s) to the Lazanda REMS program to ensure that your pharmacy management system has been successfully upgraded to allow communication with the Lazanda REMS program.

After successful completion of the test transactions, you will receive enrollment confirmation via fax or e-mail. For questions regarding the Lazanda REMS program, call 1-855-841-4234.

The Lazanda REMS Program Additional Terms and Conditions

Pharmacy ("Pharmacy") agrees to the following requirements, with respect to the Lazanda REMS Program for Lazanda (fentanyl) nasal spray (the "Program"), sponsored by Archimedes Pharma., ("Program Sponsor") and supported, under the direction of Archimedes Pharma., by NDC Health Corporation d/b/a RelayHealth ("RelayHealth") or another pharmacy transaction switch system (collectively, "Switch Systems").

Pharmacy represents that (i) it shall perform its obligations under these terms and conditions in compliance with all applicable laws and regulations, (ii) Pharmacy's participation in the Program does not conflict with its obligations under any contracts or other arrangements with any third party, and (iii) Pharmacy is authorized to submit patient information to the Switch Systems for purposes of verifying and tracking each patient's eligibility to participate in the Program, and Pharmacy authorizes Switch Systems, Program Sponsor and their agents or representatives to use the submitted information for such purposes.

Pharmacy agrees to the following Program Requirements: (a) if applicable, enable Pharmacy's pharmacy practice management system to support the Program, including submission of required data fields and display of Program messages; (b) respond appropriately to Program messages and alerts in order to comply with Program requirements, including contacting the call center when an exception process occurs; (c) report all Program Drug dispensing activity for the Program Drug NDC #s listed below to Switch Systems via submission of all billing and reversal requests.

Pharmacy acknowledges that a billing request for the Program Drug will not pass to the payer, or cash prescription processor, if the prescriber, pharmacy, or patient registration is not verified.

Program Drug	**NDC #**	**Dosage Strength**	**Unit Size**
Lazanda (fentanyl) nasal spray	51772-311-01	100 mcg	1 bottle (8 sprays)
	51772-311-04	100 mcg	4 bottles (4 x 8 sprays)
	51772-314-01	400 mcg	1 bottle (8 sprays)
	51772-314-04	400 mcg	4 bottles (4 x 8 sprays)

Pharmacy authorizes and directs the Switch Systems to de-identify, in accordance with the Health Insurance Portability and Accountability Act of 1996, as amended, its historical and prospective prescriptions claims data submitted to the Switch Systems and/or its affiliates or related to the Program on behalf of Pharmacy, and to use that de-identified data for purposes of (i) analyzing, identifying, designing, and/or enabling a REMS service;(ii) developing communication documentation for such services for both Program Sponsors and Pharmacy; and (iii) providing the Program Sponsors with reports and information (including any fees paid, which will be aggregated), for purposes of implementing, maintaining, supporting, monitoring, or improving a Program. These reports may contain information aggregated by NCPDP number. Further, Pharmacy authorizes Switch Systems to deliver all of the above enumerated data and reports otherwise to be delivered to Program Sponsor or to the agent or representative of Program Sponsor. In addition, Pharmacy authorizes Program Sponsor and its contractors Switch Systems to receive from wholesaler(s) of the Program Drug(s) distribution and purchasing data, including 867 data, with respect to the Program Drug(s).

Pharmacy acknowledges that the FDA or Program Sponsor may mandate modification, suspension, or termination of a Program. The Switch Systems reserves the right to modify, suspend, or terminate any REMS service for any reason, without liability to Switch Systems.

EXCEPT FOR SWITCH SYSTEMS' FRAUD OR INTENTIONAL MISCONDUCT ARISING OUT OF THE SERVICES OR THE PROGRAM, IN NO EVENT WILL THE PROGRAM SPONSOR OR SWITCH SYSTEMS BE LIABLE TO PHARMACY UNDER, IN CONNECTION WITH, OR RELATED TO THE PROGRAM OR THE SERVICES FOR ANY DIRECT, SPECIAL, INCIDENTAL, INDIRECT, OR CONSEQUENTIAL DAMAGES, INCLUDING, BUT NOT LIMITED TO, LOST PROFITS OR LOSS OF GOODWILL, WHETHER BASED ON BREACH OF CONTRACT, WARRANTY, TORT, PRODUCT LIABILITY, OR OTHERWISE, AND WHETHER

OR NOT SWITCH SYSTEMS OR PROGRAM SPONSOR HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGE.

To the extent any of these terms and conditions conflict with any other written agreement between the parties with respect to the Program, the terms and conditions of such other written agreement shall prevail.

If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

This form is part of an FDA-approved REMS.

The Lazanda® REMS Program Chain Pharmacy Enrollment Form

An authorized chain pharmacy representative must complete the form below. When complete, please fax the form, along with the completed Pharmacy Knowledge Assessment, to the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program at 1-855-841-4235.

I understand that Lazanda (fentanyl nasal spray) is only available through the Lazanda REMS program and I must comply with the program requirements. In addition, as the designated authorized chain pharmacy representative, I acknowledge that:

1) I have reviewed the Lazanda Full Prescribing Information and the Education Program and I have completed the Pharmacy Knowledge Assessment. I understand the risks and benefits associated with Lazanda and the requirements of the Lazanda REMS program for pharmacies.
2) I will ensure that all pharmacy staff who participate in dispensing Lazanda have been educated on the risks associated with Lazanda and the requirements of the Lazanda REMS program, as described in the Education Program. This training should be documented and is subject to audit.
3) I understand that Lazanda is not bioequivalent with other fentanyl products on a microgram-per-microgram basis and therefore must not be substituted for any other fentanyl products.
4) I understand that Lazanda is contraindicated for use in opioid non-tolerant patients.
5) I understand that the initial starting dose of Lazanda for all patients is the lowest dose (100 mcg).
6) I understand the importance of discussing the risks and benefits of Lazanda with patients and their caregivers, and in particular the importance of taking the drug as prescribed, not sharing with others, and proper disposal.
7) I understand that the Lazanda Medication Guide must be given to the patient or their caregiver each time Lazanda is dispensed.
8) I understand that Lazanda will not be dispensed without verifying through our pharmacy management system that the prescriber and pharmacy are enrolled and active, and that the patient has not been inactivated in the program.
9) I understand that ALL Lazanda prescriptions, regardless of the method of payment, must be processed through our pharmacy management system, including cash prescriptions, as well as offline plans.
10) I understand that all dispensing locations must be enrolled in the Lazanda REMS program to dispense Lazanda.
11) I understand that Lazanda can only be obtained from wholesalers/distributors that are enrolled in the Lazanda REMS program.
12) I understand that our pharmacy will not sell, loan, or transfer Lazanda inventory to any other pharmacy, institution, distributor, or prescriber.
13) I understand that our pharmacy must re-enroll in the Lazanda REMS program and successfully complete the enrollment requirements every 2 years.
14) I understand that Lazanda is only available through the REMS program. I understand that the pharmacy must comply with the Lazanda REMS program requirements for outpatient pharmacies.

Authorized Chain Pharmacy Representative Signature*: _____
Date:_____

Title:_____ First Name:_____ Last Name:_____

*For Chain pharmacy enrollment this form can be completed and signed by the authorized Chain pharmacy representative. A list of pharmacy sites that have been trained may be faxed with this enrollment form by inserting the required Pharmacy information in the last page(s) of this form. Alternatively, the list of trained pharmacy sites can be updated using the online dashboard.

Chain Pharmacy Information

Pharmacy Name:		**Chain ID:**	
Address:	**City:**	**State:**	**ZIP:**
Fax Number:	**Phone Number:**		
E-mail Address:			
Preferred Channel of Communication: E-mail …□ Fax…□			

Please fax the completed form to the Lazanda REMS program at 1-855-841-4235.
You will receive a fax or e-mail with instructions of how to submit test transaction(s) to the Lazanda REMS program to ensure that your pharmacy management system has been successfully upgraded to allow communication with the Lazanda REMS program.

After successful completion of the test transactions, you will receive enrollment confirmation via fax or email. For questions regarding the Lazanda REMS program, call 1-855-841-4234.

The Lazanda REMS Program Additional Terms and Conditions

Pharmacy ("Pharmacy") agrees to the following requirements, with respect to the Lazanda REMS Program for Lazanda (fentanyl) nasal spray (the "Program"), sponsored by Archimedes Pharma., ("Program Sponsor") and supported, under the direction of Archimedes Pharma., by NDC Health Corporation d/b/a RelayHealth ("RelayHealth") or another pharmacy transaction switch system (collectively, "Switch Systems").

Pharmacy represents that (i) it shall perform its obligations under these terms and conditions in compliance with all applicable laws and regulations, (ii) Pharmacy's participation in the Program does not conflict with its obligations under any contracts or other arrangements with any third party, and (iii) Pharmacy is authorized to submit patient information to the Switch Systems for purposes of verifying and tracking each patient's eligibility to participate in the Program and Pharmacy authorizes Switch Systems, Program Sponsor and their agents or representatives to use the submitted information for such purposes.

Pharmacy agrees to the following Program Requirements: (a) if applicable, enable Pharmacy's pharmacy practice management system to support the Program, including submission of required data fields and display of Program messages; (b) respond appropriately to Program messages and alerts in order to comply with Program requirements, including contacting the call center when an exception process occurs; (c) report all Program Drug dispensing activity for the Program Drug NDC #s listed below to Switch Systems via submission of all billing and reversal requests.

Pharmacy acknowledges that a billing request for the Program Drug will not pass to the payer, or cash prescription processor, if the prescriber, pharmacy, or patient registration is not verified.

Program Drug	**NDC #**	**Dosage Strength**	**Unit Size**

Lazanda (fentanyl) nasal spray	51772-311-01	100 mcg	1 bottle (8 sprays)
	51772-311-04	100 mcg	4 bottles (4 x 8 sprays)
	51772-314-01	400 mcg	1 bottle (8 sprays)
	51772-314-04	400 mcg	4 bottles (4 x 8 sprays)

Pharmacy authorizes and directs the Switch Systems to de-identify, in accordance with the Health Insurance Portability and Accountability Act of 1996, as amended, its historical and prospective prescriptions claims data submitted to the Switch Systems and/or its affiliates in connection with to the Program on behalf of Pharmacy, and to use that de-identified data for purposes of (i) analyzing, identifying, designing, and/or enabling a REMS service;(ii) developing communication documentation for such services for both Program Sponsors and Pharmacy; and (iii) providing the Program Sponsors with reports and information (including any fees paid, which will be aggregated), for purposes of implementing, maintaining, supporting, monitoring, or improving a Program. These reports may contain information aggregated by NCPDP number. Further, Pharmacy authorizes Switch Systems to deliver all of the above enumerated data and reports otherwise to be delivered to Program Sponsor or to the agent or representative of Program Sponsor. In addition, Pharmacy authorizes Program Sponsor and its contractors Switch Systems to receive from wholesaler(s) of the Program Drug(s) distribution and purchasing data, including 867 data, with respect to the Program Drug(s).

Pharmacy acknowledges that the FDA or Program Sponsor may mandate modification, suspension, or termination of a Program. The Switch Systems reserves the right to modify, suspend, or terminate any REMS service for any reason, without liability to Switch Systems.

EXCEPT FOR SWITCH SYSTEMS' FRAUD OR INTENTIONAL MISCONDUCT ARISING OUT OF THE SERVICES OR THE PROGRAM, IN NO EVENT WILL THE PROGRAM SPONSOR OR SWITCH SYSTEMS BE LIABLE TO PHARMACY UNDER, IN CONNECTION WITH, OR RELATED TO THE PROGRAM OR THE SERVICES FOR ANY DIRECT, SPECIAL, INCIDENTAL, INDIRECT, OR CONSEQUENTIAL DAMAGES, INCLUDING, BUT NOT LIMITED TO, LOST PROFITS OR LOSS OF GOODWILL, WHETHER BASED ON BREACH OF CONTRACT, WARRANTY, TORT, PRODUCT LIABILITY, OR OTHERWISE, AND WHETHER OR NOT SWITCH SYSTEMS OR PROGRAM SPONSOR HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGE.

To the extent any of these terms and conditions conflict with any other written agreement between the parties with respect to the Program, the terms and conditions of such other written agreement shall prevail.

If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

This form is part of an FDA-approved REMS.

List of Pharmacy Sites that have been Trained According to Lazanda REMS Requirements
(continue on a separate page(s) if required)

Pharmacy Name*:		**Chain ID:**	
Address*:	**City:**	**State:**	**ZIP:**
Fax Number:		**Phone Number:**	
E-mail Address:			
Preferred Channel of Communication: E-mail …☐ Fax…☐			

Pharmacy Name*:		**Chain ID:**	
Address*:	**City:**	**State:**	**ZIP:**
Fax Number:		**Phone Number:**	
E-mail Address:			
Preferred Channel of Communication: E-mail …☐ Fax…☐			

Pharmacy Name*:		**Chain ID:**	
Address*:	**City:**	**State:**	**ZIP:**
Fax Number:		**Phone Number:**	
E-mail Address:			
Preferred Channel of Communication: E-mail …☐ Fax…☐			

Pharmacy Name*:		**Chain ID:**	
Address*:	**City:**	**State:**	**ZIP:**
Fax Number:		**Phone Number:**	
E-mail Address:			
Preferred Channel of Communication: E-mail …☐ Fax…☐			

Appendix J: Lazanda REMS Inpatient Pharmacy Enrollment Form

[Logo] **Lazanda® (fentanyl) nasal spray**

The Lazanda® REMS Program Inpatient Pharmacy Enrollment Form

The authorized responsible site pharmacist must complete the form below. When complete, please fax the form, along with the completed Pharmacy Knowledge Assessment, to the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program at 1-855-841-4235.

I understand that Lazanda (fentanyl nasal spray) is only available through the Lazanda REMS program and I must comply with the program requirements. In addition, as the designated authorized pharmacist, I acknowledge that:

1) I have reviewed the Lazanda Full Prescribing Information and the Education Program and I have completed the Pharmacy Knowledge Assessment. I understand the benefits and risks associated with Lazanda and the requirements of the Lazanda REMS program.
2) I will ensure that our inpatient pharmacists are educated on the risks associated with Lazanda and the requirements of the Lazanda REMS program, as described in the Education Program.
3) I understand that Lazanda is not bioequivalent to other fentanyl products on a microgram-per-microgram basis and therefore must not be substituted for other fentanyl products.
4) I understand that Lazanda is contraindicated for use in opioid non-tolerant patients.
5) I understand that the initial starting dose of Lazanda for all patients is the lowest dose (100 mcg).
6) I understand that pharmacies within or associated with the healthcare facility that dispense to outpatients must also be enrolled in and comply with the Lazanda REMS program to dispense Lazanda to outpatients.
7) I understand that our inpatient pharmacy is not to dispense Lazanda for outpatient use.
8) I understand that a prescriber who wants to discharge a patient with a Lazanda prescription, intended to be dispensed by an outpatient pharmacy, will be required to enroll in the REMS program.
9) I will establish or oversee the establishment of a system, order sets, protocols, and/or other measures to help ensure appropriate patient selection and compliance with the requirements of the Lazanda REMS.
10) I understand that our pharmacy will not sell, loan, or transfer Lazanda inventory to any other pharmacy, institution, distributor, or prescriber.
11) I understand that Lazanda can only be obtained from wholesalers/distributors that are enrolled in the Lazanda REMS program.
12) I understand that our pharmacy must re-enroll in the Lazanda REMS program every 2 years.
13) I understand that Lazanda is available only through the Lazanda REMS program. I understand and agree to comply with the Lazanda REMS program requirements for inpatient pharmacies.

Authorized Pharmacist Signature: _____Date: _____

Title:_____ First Name:_____ Last Name:_____

Inpatient Pharmacy Information

Pharmacy Name:			
Address:			
City:		**State:**	**ZIP:**
State Pharmacy License Number:	**License State:**		
Phone Number:	**Fax Number:**		
DEA Number:	**E-mail Address:**		
Preferred Channel of Communication: E-mail …□ Fax…□			
If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.			

This form is part of an FDA-approved REMS.

Appendix K: Lazanda REMS Pharmacy Overviews

The Lazanda® REMS Program - An Overview for Outpatient Pharmacies

This overview is part of an FDA-approved REMS.

What Is Lazanda®?

Lazanda is a fentanyl nasal spray indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain**.

What Is the Lazanda REMS Program?

The Lazanda Risk Evaluation and Mitigation Strategy (REMS) program is designed to ensure informed risk-benefit decisions before initiating treatment, and while patients are on treatment, to ensure appropriate use of Lazanda. Because of the risk for misuse, abuse, addiction, and overdose, Lazanda is available only through a REMS program required by the Food and Drug Administration. Under the Lazanda REMS program, only prescribers, pharmacies, distributors, and patients enrolled in the program are able to prescribe, dispense, distribute, and receive Lazanda, respectively, in an outpatient setting. Inpatient prescribing of Lazanda is detailed in *An Overview for Inpatient Pharmacies.*

Outpatient Pharmacy Enrollment

In order to reduce the risks of inappropriate patient selection and ensure appropriate dosing and administration of Lazanda, your pharmacy will need to be enrolled in the Lazanda REMS program. Enrollment requires the authorized pharmacist at the pharmacy to complete the Lazanda REMS Education Program and Pharmacy Knowledge Assessment on behalf of the pharmacy. The authorized pharmacist must acknowledge that they will train all other pharmacy staff involved in the dispensing of Lazanda.

The Education Program is available online at the Lazanda REMS program website (www.LazandaREMS.com) or by contacting the Lazanda REMS call center at 1-855-841-4234. Once the education program and knowledge assessment are completed, the authorized pharmacist, on behalf of the pharmacy, will be required to attest to their understanding of the appropriate use of Lazanda and adherence to the Lazanda REMS program requirements. Supply of Lazanda to pharmacies is controlled by enrolled distributors, who will verify current enrollment of the pharmacy in the Lazanda REMS program before shipping Lazanda. Pharmacies will be required to re-enroll in the Lazanda REMS program every 2 years.

Only enrolled pharmacies will be eligible to purchase or dispense Lazanda. In addition, pharmacies can only dispense prescriptions if the patient and the prescriber are enrolled in the Lazanda REMS program. Patients will be automatically enrolled in Lazanda REMS upon processing of their first Lazanda prescription. If the patient and/or the prescriber are not enrolled in the Lazanda REMS program, the Lazanda prescription will not be authorized by the Lazanda REMS program and should not be dispensed to the patient.

Prescribers, pharmacies, and patients are required to acknowledge their understanding of the potential risks involved with inappropriate use of Lazanda. Prescribers and pharmacies should ensure:

- Completion of the relevant education program and knowledge assessment, and submission of the relevant enrollment forms to the Lazanda REMS program.
- Appropriate patient selection.

- Completion and submission of a Patient-Prescriber Agreement to the Lazanda REMS program.
- That patients are provided with relevant Lazanda REMS program materials and educated on the benefits and risks of treatment with Lazanda.

Overview of Steps for the Lazanda REMS Program

Step 1. Pharmacy Education, Pharmacy Management Systems, and Enrollment

- Review the Lazanda REMS Education Program and successfully complete the Pharmacy Knowledge Assessment.
- Ensure the pharmacy enables their pharmacy management system to support communication with the Lazanda REMS system, using established telecommunication standards, and runs the standardized validation test transaction to validate the system enhancements.
- Complete and sign the Outpatient Pharmacy Enrollment Form.
- Receive a secure user name and password to be able to access the Lazanda REMS program.
- Re-enroll every 2 years.

Step 2. Training Other Pharmacy Staff

- Ensure that all pharmacy staff involved in the processing and dispensing of Lazanda have been trained to only dispense Lazanda in accordance with the Lazanda REMS program requirements.
- Ensure that this training is documented and retained by the pharmacy. This documentation should include the pharmacist/pharmacy staff member's name, the date training was completed, and the method of training, as a minimum.

Step 3. Enrollment Confirmation

- Confirm the prescriber and patient are enrolled in the Lazanda REMS program with each prescription by submitting a pharmacy billing claim from your pharmacy practice management system. Submitting a claim for a patient's first Lazanda prescription through the pharmacy management system will automatically enroll that patient in the Lazanda REMS program.
- To allow the REMS system to confirm prescriber and patient enrollment, you must populate the following fields in the pharmacy billing claim:
    - Patient First Name.
    - Patient Last Name.
    - Patient Date of Birth.
    - Patient ZIP / Postal Zone.
    - Quantity Dispensed.
    - Days Supply.
    - Prescriber ID.
    - Prescriber Last Name.

- If the prescriber or patient enrollment is not validated, contact the Lazanda REMS call center at 1-855-841-4234 for further instruction.

Step 4. Dispensing

- Receive approval and an authorization ID number from the Lazanda REMS program, and then prepare, label, and dispense medication.

Step 5. Counseling Patients and Provision of Medication Guide

- Advise the patient on how to take, store, and dispose of Lazanda appropriately.
- Provide a copy of the Medication Guide to the patient with each prescription.

Step 6. Monitoring

- Promptly report suspected adverse events including misuse, abuse, addiction, and overdose directly to Archimedes Pharma by calling 1-866-435-6775.
- Respond to requests for additional information from the Lazanda REMS program.

For more information, you can call the Lazanda REMS program at 1-855-841-4234 or visit www.LazandaREMS.com.

Important Safety Information

Boxed Warnings

[BEGIN BOX]

WARNINGS: POTENTIAL FOR ABUSE and IMPORTANCE OF PROPER PATIENT SELECTION

Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. Lazanda can be abused in a manner similar to other opioid agonists. Consider this potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion. Schedule II opioid substances, which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with other transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients) and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

Lazanda is indicated only for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine/daily, or at least 25 mcg transdermal fentanyl/hour, or at least 30 mg of oral oxycodone daily, or at least 8 mg oral hydromorphone daily, at least 25 mg oral oxymorphone daily or an equianalgesic dose of another opioid for a week or longer.

Lazanda is contraindicated in opioid non-tolerant patients and is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl product to Lazanda. Patients beginning treatment with Lazanda must begin with titration from the 100 mcg dose.

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda.

Lazanda is intended to be used only in the care of opioid tolerant patients with cancer and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda contains a medicine in an amount that can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times.

The concomitant use of Lazanda with cytochrome P450 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

[END BOX]

Adverse Reactions

The most commonly observed adverse events seen with Lazanda are typical of opioid side effects, such as nausea, constipation, somnolence, and headache. Expect opioid side effects and manage them accordingly.

Further Information

If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

www.LazandaREMS.com

The Lazanda® REMS Program - An Overview for Chain Pharmacies

This overview is part of an FDA-approved REMS.

The Lazanda® REMS Program - An Overview for Chain Pharmacies

What Is Lazanda®?

Lazanda is a fentanyl nasal spray indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain**.

What Is the Lazanda REMS Program?

The Lazanda Risk Evaluation and Mitigation Strategy (REMS) program is designed to ensure informed risk-benefit decisions before initiating treatment, and while patients are on treatment, to ensure appropriate use of Lazanda. Because of the risk for misuse, abuse, addiction, and overdose, Lazanda is available only through a REMS program required by the Food and Drug Administration. Under the Lazanda REMS program, only prescribers, pharmacies, distributors, and patients enrolled in the program are able to prescribe, dispense, distribute, and receive Lazanda, respectively, in an outpatient setting. Inpatient prescribing of Lazanda is detailed in *An Overview for Inpatient Pharmacies.*

Chain Pharmacy Enrollment

In order to reduce the risks of inappropriate patient selection and to ensure appropriate dosing and administration of Lazanda, the chain pharmacy with an authorized chain pharmacy representative will need to be enrolled in the Lazanda REMS program. Enrollment requires an authorized chain pharmacy representative to complete the Lazanda REMS Education Program and Knowledge Assessment on behalf of the chain.

The authorized chain pharmacy representative must acknowledge that training will occur for all pharmacy staff involved in the dispensing of Lazanda. The Education Program is available online at the Lazanda REMS program website (www.LazandaREMS.com) or by contacting the Lazanda REMS call center at 1-855-841-4234. Once the Education Program and Knowledge Assessment are completed, the authorized chain pharmacy representative, on behalf of the chain, will be required to attest to their understanding of the appropriate use of Lazanda and adherence to the Lazanda REMS program requirements.

Supply of Lazanda to pharmacies is controlled by enrolled distributors, who will verify the current enrollment status of the pharmacy within the chain in the Lazanda REMS program before shipping Lazanda. The chain will be required to re-enroll in the Lazanda REMS program every 2 years.

Only enrolled chain pharmacies will be eligible to purchase or dispense Lazanda. In addition, outpatient pharmacies can only dispense prescriptions if the patient and the prescriber are enrolled in the Lazanda REMS program. Patients will be automatically enrolled in the Lazanda REMS upon processing of their first Lazanda prescription. If the patient and/or the prescriber are not enrolled in the Lazanda REMS program, the Lazanda prescription will not be authorized by the Lazanda REMS program, the chain pharmacy will receive a rejection message, and the prescription will not be dispensed to the patient.

Prescribers, pharmacies, and patients are required to acknowledge their understanding of the potential risks involved with inappropriate use of Lazanda. Prescribers and pharmacies should ensure:

- Completion of the relevant education program and knowledge assessment, and submission of the relevant enrollment forms to the Lazanda REMS program.
- Appropriate patient selection.
- Completion and submission of a Patient-Prescriber Agreement to the Lazanda REMS program.
- That patients are provided with relevant Lazanda REMS program materials and educated on the benefits and risks of treatment with Lazanda.

Overview of Steps for the Lazanda REMS Program for Chain Pharmacies

Step 1. Chain Pharmacy Education, Pharmacy Management Systems, and Enrollment –

- Review the Lazanda REMS Education Program and successfully complete the Pharmacy Knowledge Assessment.
- Ensure the pharmacy enables their pharmacy management system to support communication with the Lazanda REMS system, using established telecommunication standards, and runs the standardized validation test transaction to validate the system enhancements.
- Complete and sign the Chain Pharmacy Enrollment Form.
- Receive a secure user name and password to be able to access the Lazanda REMS program.
- Re-enroll every 2 years.

Step 2. Training Other Pharmacy Staff

- Ensure that all pharmacy staff involved in the processing and dispensing of Lazanda have been trained to only dispense Lazanda in accordance with the Lazanda REMS program requirements.
- Ensure that this training is documented and retained by the pharmacy. This documentation should include the pharmacist/pharmacy staff member name(s), the date training was completed, and the method of training, as a minimum.
- A list of pharmacy sites that have been trained may be faxed with the enrollment form or updated using the online dashboard. This list should include the required Pharmacy Information for each pharmacy site.

Step 3. Enrollment Confirmation

- Confirm that the prescriber and patient are enrolled in the Lazanda REMS program with each prescription by submitting a pharmacy billing claim from your pharmacy practice management system. Submitting a claim for a patient's first Lazanda prescription through the pharmacy management system will automatically enroll that patient in the Lazanda REMS program.
- To allow the REMS system to confirm prescriber and patient enrollment, you must populate the following fields in the pharmacy billing claim:
  - Patient First Name.
  - Patient Last Name.

- — Patient Date of Birth.
- — Patient ZIP / Postal Zone.
- — Quantity Dispensed.
- — Days Supply.
- — Prescriber ID.
- — Prescriber Last Name.

- If the prescriber or patient enrollment is not validated, or if any other rejection message is received that prevents the prescription being filled, contact the Lazanda REMS call center at 1-855-841-4234 for further instruction.

Step 4. Dispensing

- Receive approval and an authorization ID number from the Lazanda REMS program and then prepare, label, and dispense the medication.

Step 5. Counseling patients and provision of Medication Guide

- Advise the patient on how to take, store, and dispose of Lazanda appropriately.
- Provide a copy of the Medication Guide to the patient with each prescription.

Step 6. Monitoring

- Promptly report suspected adverse events, including misuse, abuse, addiction, and overdose, directly to the Lazanda REMS program at 1-855-841-4234. You also may report adverse event information to the FDA MedWatch Reporting System by telephone at (800) FDA-1088 or by mail using Form 3500, available at www.fda.gov/medwatch.
- Respond to requests for additional information from the Lazanda REMS program.

For more information, you can call the Lazanda REMS program at 1-855-841-4234 or visit www.LazandaREMS.com

This overview is part of an FDA-approved Lazanda REMS.

Important Safety Information

Boxed Warnings

[BEGIN BOX]

WARNINGS: POTENTIAL FOR ABUSE and IMPORTANCE OF PROPER PATIENT SELECTION

Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. Lazanda can be abused in a manner similar to other opioid agonists. Consider this potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion. Schedule II opioid substances, which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with other transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients) and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

Lazanda is indicated only for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine/daily, or at least 25 mcg transdermal fentanyl/hour, or at least 30 mg of oral oxycodone daily, or at least 8 mg oral hydromorphone daily, at least 25 mg oral oxymorphone daily or an equianalgesic dose of another opioid for a week or longer.

Lazanda is contraindicated in opioid non-tolerant patients and is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl product to Lazanda. Patients beginning treatment with Lazanda must begin with titration from the 100 mcg dose.

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda.

Lazanda is intended to be used only in the care of opioid tolerant patients with cancer and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda contains a medicine in an amount that can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times.

The concomitant use of Lazanda with cytochrome P450 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

[END BOX]

Adverse Reactions

The most commonly observed adverse events seen with Lazanda are typical of opioid side effects, such as nausea, constipation, somnolence, and headache. Expect opioid side effects and manage them accordingly.

Further Information

If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

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www.LazandaREMS.com
Lazanda® is a trademark of Archimedes Development Ltd.

The Lazanda® REMS Program - An Overview for Inpatient Pharmacies

This overview is part of an FDA-approved REMS.

What Is Lazanda®?

Lazanda is a fentanyl nasal spray indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain**.

What Is the Lazanda REMS Program?

The Lazanda Risk Evaluation and Mitigation Strategy (REMS) program is designed to ensure informed risk-benefit decisions before initiating treatment, and while patients are on treatment, to ensure appropriate use of Lazanda (fentanyl) nasal spray. Because of the risk for misuse, abuse, addiction, and overdose, Lazanda is available only through a REMS program required by the Food and Drug Administration. In order for inpatient pharmacies (eg, hospitals, hospices, and long-term care facilities) to dispense Lazanda for inpatient use only, the inpatient pharmacy must be enrolled in the Lazanda REMS program. For inpatient administration of Lazanda, patient and prescriber enrollment in the Lazanda REMS program is not required.

Inpatient Pharmacy Enrollment

An authorized pharmacist representing an inpatient pharmacy in a healthcare facility will need to review the Lazanda REMS Education Program, successfully complete the Pharmacy Knowledge Assessment, and enroll the inpatient pharmacy in the Lazanda REMS program. The Education Program is available online at the Lazanda REMS program website (www.LazandaREMS.com) or by contacting the Lazanda REMS call center at 1-855-841-4234. Once the education program and knowledge assessment are completed, the authorized pharmacist will attest to their understanding of the appropriate use of Lazanda and adherence to the Lazanda REMS program requirements, on behalf of their inpatient pharmacy.

Product supply of Lazanda to the inpatient pharmacy will be controlled by enrolled distributors. Enrolled distributors will verify current enrollment of the inpatient pharmacy in the Lazanda REMS program, before shipping Lazanda. Unless enrolled in the Lazanda REMS program, the inpatient pharmacy will not be eligible to purchase or dispense Lazanda. Inpatient pharmacies (authorized pharmacist) will be required to re-enroll in the Lazanda REMS program every 2 years.

Inpatient Prescribers

Prescribers at inpatient facilities do not need to enroll in the Lazanda REMS program to have Lazanda dispensed to their patients who are being treated on an inpatient basis.

Outpatient Use

If a prescriber wants to discharge a patients with a Lazanda prescription, intended to be dispensed by an outpatient pharmacy, the prescriber will need to enroll in the Lazanda REMS program. Patients will be automatically enrolled in the Lazanda REMS upon processing of their first Lazanda prescription.

Outpatient pharmacies, within or associated with the healthcare facility, that provide dispensing services to outpatients must also be separately enrolled in the Lazanda REMS program and comply with the Lazanda REMS program to dispense Lazanda to outpatients (See *An Overview for Outpatient Pharmacies*).

Overview of Steps for the Lazanda REMS Program for Inpatient Pharmacies

Step 1. Select an Authorized Inpatient Pharmacist

- The representative is authorized by the inpatient pharmacy to establish and oversee the Lazanda REMS program requirements within the inpatient healthcare facility.

Step 2. Complete Lazanda REMS Education Program

- The authorized pharmacist must successfully complete the Lazanda REMS Education Program and Pharmacy Knowledge Assessment.

Step 3. Enroll

- The inpatient authorized pharmacist must enroll in the Lazanda REMS program by completing the Lazanda REMS program Inpatient Pharmacy Enrollment Form and re-enroll every 2 years.
- To enroll, access the Lazanda REMS program website at www.LazandaREMS.com. If you are unable to enroll online, please call the Lazanda REMS program call center at 1-855-841-4234 for further assistance.

Step 4. Implement

- The inpatient authorized pharmacist must establish or oversee the system, order sets, protocols, and/or other measures to help ensure appropriate patient selection and compliance with the requirements of the Lazanda REMS program.
- The inpatient authorized pharmacist must ensure that inpatient pharmacists are educated on the risks associated with Lazanda and the requirements of the Lazanda REMS program, as described in the Education Program.
- The inpatient authorized pharmacist must ensure that the inpatient pharmacy does not sell, loan, or transfer Lazanda inventory to any other pharmacy, institution, distributor, or prescriber.
- Inpatient pharmacies may not dispense Lazanda for outpatient use.

Step 5. Monitoring

- Ensure that suspected adverse events, including misuse, abuse, addiction, and overdose, are promptly reported directly to Archimedes Pharma by calling 1-866-435-6775.
- Respond to requests for additional information from the Lazanda REMS program.

For more information on the REMS program, you can call the Lazanda REMS program at 1-855-841-4234 or visit www.LazandaREMS.com.

Important Safety Information

Boxed Warnings

[BEGIN BOX]
WARNINGS: POTENTIAL FOR ABUSE and IMPORTANCE OF PROPER PATIENT SELECTION

Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. Lazanda can be abused in a manner similar to other opioid agonists. Consider the potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion. Schedule II opioid substances, which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with other transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients) and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

Lazanda is indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine/daily, or at least 25 mcg transdermal fentanyl/hour, or at least 30 mg of oral oxycodone daily, or at least 8 mg oral hydromorphone daily, at least 25 mg oral oxymorphone daily or an equianalgesic dose of another opioid for a week or longer.

Lazanda is contraindicated in opioid non-tolerant patients and is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl product to Lazanda. Patients beginning treatment with Lazanda must begin with titration from the 100 mcg dose.

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda.

Lazanda is intended to be used only in the care of opioid tolerant patients with cancer and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda® contains a medicine in an amount that could be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times.

The concomitant use of Lazanda with cytochrome P450 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

[END BOX]

Adverse Reactions

The most commonly observed adverse events seen with Lazanda are typical of opioid side effects, such as nausea, constipation, somnolence, and headache. Expect opioid side effects and manage them accordingly.

Further Information

If you have any questions or require additional information or further copies of all Lazanda REMS documents, please visit www.LazandaREMS.com, or call the Lazanda REMS program at 1-855-841-4234.

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www.LazandaREMS.com
Lazanda® is a trademark of Archimedes Development Ltd.

Bedminster, NJ 07921

Appendix L: Lazanda REMS Dear Pharmacy Letters

Important Drug Warning
Subject: Risk of misuse, abuse, addiction, and overdose for Lazanda® (fentanyl) nasal spray; FDA-required restricted-distribution program

Dear Outpatient Pharmacy:

Archimedes Pharma would like to inform you of the approval of Lazanda (fentanyl) nasal spray, a treatment for breakthrough pain (BTPc) in opioid-tolerant cancer patients. Because of the potential risk for misuse, abuse, addiction, and overdose, Lazanda is only available through the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program. In an outpatient setting, only prescribers, pharmacies, distributors, and patients enrolled in the program are able to prescribe, dispense, distribute, and receive Lazanda, respectively, under the Lazanda REMS program.

Lazanda is an opioid analgesic indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain**.

Patients considered opioid tolerant are those who are taking at least 60 mg oral morphine/day; 25 mcg transdermal fentanyl/hour; 30 mg oral oxycodone/day; 8 mg oral hydromorphone/day; 25 mg oral oxymorphone/day; or an equianalgesic dose of another opioid for 1 week or longer.

In order for an outpatient pharmacy to take part in the Lazanda REMS program, and dispense Lazanda, an authorized pharmacist must:

- Review the Education Program and the Lazanda Full Prescribing Information.
- Successfully complete the Pharmacy Knowledge Assessment.
- Complete the Pharmacy Enrollment Form.
- Ensure the pharmacy management system supports communication with the Lazanda REMS system.
- Re-enroll every 2 years.

To enroll in the Lazanda REMS program, visit www.LazandaREMS.com or call 1-855-841-4234.

Lazanda REMS
The goals of the Lazanda REMS are to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors by:

1. Prescribing and dispensing Lazanda only to appropriate patients, which includes **use only in opioid-tolerant patients**.
2. Preventing inappropriate conversion between fentanyl products.
3. Preventing accidental exposure to children and others for whom it was not prescribed.
4. Educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose.

Important Safety Information

Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. Lazanda can be abused in a manner similar to other opioid anagonists, legal or illicit. Consider the potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion. Schedule II opioid substances which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with other oral transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (eg, use in opioid non-tolerant patients), and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

Lazanda is contraindicated in opioid non-tolerant patients and is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl product to Lazanda. Patients starting treatment with Lazanda must begin titration with the 100 mcg dose.

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda.

Lazanda is intended to be **used only in the care of opioid-tolerant patients with cancer** and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda contains a medicine in an amount that can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times.

The concomitant use of Lazanda with cytochrome P450 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

Adverse Reactions
The most commonly observed adverse events seen with Lazanda are typical of opioid side effects, such as nausea, constipation, somnolence, and headache. Expect opioid side effects and manage them accordingly.
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Medication Guide
It is an FDA requirement to distribute a copy of the enclosed Medication Guide to each patient with each prescription filled for Lazanda. A Medication Guide will be provided with every carton of Lazanda. If you require additional Medication Guides, you can:

- Print copies from the Lazanda REMS program website at www.LazandaREMS.com.
- Contact the Lazanda REMS program by calling 1-855-841-4234.

Adverse Event Reporting
Prescribers should report all adverse events associated with the use of Lazanda directly to Archimedes Pharma at 1-866-435-6775.

Further Information
If you have questions about the Lazanda REMS program, please visit www.LazandaREMS.com for more information or call the toll-free number, 1-855-841-4234.
If you have any questions about Lazanda itself, contact Archimedes Pharma at 1-866-435-6775.

Thank you,

Linda Wase, MD
Senior Vice President & Chief Medical Officer, Archimedes Pharma

This letter is part of an FDA-approved REMS.

Important Drug Warning
Subject: Risk of misuse, abuse, addiction, and overdose for Lazanda® (fentanyl) nasal spray; FDA-required restricted-distribution program

Dear Inpatient Pharmacy:

Archimedes Pharma would like to inform you of the approval of Lazanda (fentanyl) nasal spray, a treatment for breakthrough pain (BTPc) in opioid-tolerant cancer patients. Because of the potential risk for misuse, abuse, addiction, and overdose, Lazanda is only available through the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program. Inpatient pharmacies should not dispense for outpatient use. If Lazanda is prescribed and dispensed to outpatients in your Healthcare Facility, you must enroll your inpatient pharmacy in the Lazanda REMS program.

Lazanda is an opioid analgesic indicated only for the management of breakthrough pain in cancer patients, 18 years of age and older, **who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain**.

Patients considered opioid tolerant are those who are taking at least: 60 mg oral morphine/day; 25 mcg transdermal fentanyl/hour; 30 mg oral oxycodone/day; 8 mg oral hydromorphone/day; 25 mg oral oxymorphone/day; or an equianalgesic dose of another opioid for 1 week or longer.

In order for an inpatient pharmacy to dispense Lazanda, an authorized pharmacist must:

- Review the Pharmacy Education Program and Lazanda full Prescribing Information.
- Successfully complete the Pharmacy Knowledge Assessment.
- Complete the Pharmacy Enrollment Form.
- Re-enroll every 2 years.

For inpatient administration of Lazanda, patient and prescriber enrollment in the Lazanda REMS program are not required.

To enroll in the Lazanda REMS program, visit www.LazandaREMS.com or call 1-855-841-4234.

Lazanda REMS
The goals of the Lazanda REMS are to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors by:

5. Prescribing and dispensing Lazanda only to appropriate patients, which includes **use only in opioid-tolerant patients**.
6. Preventing inappropriate conversion between fentanyl products.
7. Preventing accidental exposure to children and others for whom it was not prescribed.
8. Educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose.

Important Safety Information

Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. Lazanda can be abused in a manner similar to other opioid agonists, legal or illicit. Consider the potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion. Schedule II opioid substances which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with other oral transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (eg, use in opioid non-tolerant patients), and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

Lazanda is contraindicated in opioid non-tolerant patients and is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

When prescribing, do not convert patients on a microgram-per-microgram basis from another fentanyl product to Lazanda. Patients starting treatment with Lazanda must begin titration with the 100 mcg dose.

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda.

Lazanda is intended to be **used only in the care of opioid-tolerant patients with cancer** and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda contains a medicine in an amount that can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times.

The concomitant use of Lazanda with cytochrome P450 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

Adverse Reactions
The most commonly observed adverse events seen with Lazanda are typical of opioid side effects, such as nausea, constipation, somnolence, and headache. Expect opioid side effects and manage them accordingly.

Adverse Event Reporting
Inpatient Healthcare Facilities should report all adverse events associated with the use of Lazanda directly to Archimedes Pharma at 1-866-435-6775.

Please see the attached Full Prescribing Information, including boxed warnings, and Medication Guide for important safety information for Lazanda.

Further Information
If you have questions about the Lazanda REMS program, please visit www.LazandaREMS.com for more information or call the toll-free number, 1-855-841-4234.
If you have any questions about Lazanda itself, contact Archimedes Pharma at 1-866-435-6775.

Thank you,

Linda Wase, MD
Senior Vice President & Chief Medical Officer, Archimedes Pharma

This letter is part of an FDA-approved REMS.

Appendix M: Lazanda REMS Dear Distributor Letter

Dear Distributor:

Archimedes Pharma would like to inform you of the approval of Lazanda® (fentanyl) nasal spray, a treatment for breakthrough pain (BTPc) in opioid-tolerant patients. Because of the risk for misuse, abuse, addiction, and overdose, Lazanda is only available through the Lazanda Risk Evaluation and Mitigation Strategy (REMS) program, a restricted-distribution program. Under the Lazanda REMS program, only prescribers, pharmacies, distributors, and patients enrolled in the program are able to prescribe, dispense, distribute, and receive Lazanda, respectively.

The goals of the Lazanda REMS are to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors by:

1. Prescribing and dispensing Lazanda only to appropriate patients, which includes **use only in opioid-tolerant patients**.
2. Preventing inappropriate conversion between fentanyl products.
3. Preventing accidental exposure to children and others for whom it was not prescribed.
4. Educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose.

Distributor Responsibilities for the Lazanda REMS program

In order to meet the goals of the Lazanda REMS, distributors must verify current enrollment of a pharmacy in the Lazanda REMS program before distributing Lazanda. If the pharmacy is not enrolled, the distributor should not fill any orders for Lazanda until enrollment is confirmed. The Lazanda REMS program maintains a database of enrolled pharmacies.

As part of the Lazanda REMS program, distributors will need to confirm their understanding of the Lazanda REMS program as it relates to distributors, by reading and signing the enclosed Lazanda REMS program Distributor Enrollment Form.

Please note that Archimedes Pharma cannot ship Lazanda to any distributors who have not completed and signed the Distributor Enrollment Form. Once completed, please fax the enrollment form to the Lazanda REMS program at 1-855-841-4235 to enable you to start ordering Lazanda.

Distributor Overview of Steps for the Lazanda REMS Program

Step 1. Distributor Enrollment in the Lazanda REMS Program

- Review and understand the requirements of the Lazanda REMS program.
- Verify ability to comply with program requirements.
- Verify that relevant staff are trained on the Lazanda REMS program procedures.
- Complete the Distributor Enrollment Form (distributors will be required to re-enroll every 2 years).
- Fax Distributor Enrollment Form to the Lazanda REMS program at 1-855-841-4235.
- Receive log-in information (secure user name and password) to access the Lazanda REMS program website and the secure ftp site for pharmacy and enrollment verification.

Step 2. Verification of Lazanda REMS Program Pharmacy Enrollment Prior to Distributing Lazanda

- Obtain the current list of enrolled pharmacies after enrollment by:
  - Downloading (daily) from a secure ftp site.
  - Accessing the website (www.LazandaREMS.com) using a password.
  - Calling the Lazanda REMS call center at 1-855-841-4234.
- Ensure that pharmacies are enrolled in the Lazanda REMS program before distributing Lazanda.
- If a pharmacy wants to place an order for Lazanda, but is not listed on the enrolled list for the Lazanda REMS program, do not distribute Lazanda. Instruct the pharmacy that they will need to become enrolled in the Lazanda REMS program in order to purchase Lazanda.

Step 3. Provide Periodic Distribution Data

- Provide data to the Lazanda REMS program, including information on shipments, to ensure shipments are only made to enrolled pharmacies.

Lazanda is available in 2 strengths, each having a distinctive packaging color and marking.

Product Description	NDC #	Dosage Strength	Unit Size
Lazanda (fentanyl) nasal spray	51772-311-01	100 mcg	1 bottle (8 sprays)
	51772-311-04	100 mcg	4 bottles (4 x 8 sprays)
	51772-314-01	400 mcg	1 bottle (8 sprays)
	51772-314-04	400 mcg	4 bottles (4 x 8 sprays)

Adverse Event Reporting

Distributors should report any adverse events associated with the use of Lazanda directly to Archimedes Pharma by calling 1-866-435-6775. Please see enclosed Full Prescribing Information for more information about Lazanda.

Thank you,

The Lazanda REMS Team

Enclosures: Full Prescribing Information, Distributor Enrollment Form.

This letter is part of an FDA-approved REMS.

Appendix N: Lazanda REMS Distributor Enrollment Form

Lazanda® (fentanyl) nasal spray

The Lazanda® REMS Program Distributor Enrollment Form

Lazanda is fentanyl in a nasal spray, available only through the REMS program called Lazanda Risk Evaluation and Mitigation Strategy (REMS), a restricted-distribution program. Under the Lazanda REMS program, only prescribers, pharmacies, distributors, and patients enrolled in the program are able to prescribe, dispense, distribute, and receive Lazanda, respectively.

The goals of the Lazanda REMS are to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors by:

1. Prescribing and dispensing Lazanda only to appropriate patients, which includes **use only in opioid-tolerant patients**.
2. Preventing inappropriate conversion between fentanyl products.
3. Preventing accidental exposure of children and others for whom it was not prescribed.
4. Educating prescribers, pharmacists, and patients on the potential for misuse, abuse, addiction, and overdose.

Under the Lazanda REMS program, distributors must verify current enrollment of a pharmacy in the Lazanda REMS program before distributing Lazanda to that pharmacy. If the pharmacy is not enrolled, the distributor will not fill any orders for Lazanda until enrollment is confirmed. The current list of enrolled pharmacies may be accessed as a daily download from a secure ftp site, from a password-protected section of the website (www.LazandaREMS.com), or by calling 1-855-841-4234 after enrollment.

Distributor Enrollment

I understand that Lazanda (fentanyl) nasal spray is only available through the Lazanda REMS program and I must comply with the program requirements and acknowledge that:

1. I will ensure that relevant staff are trained on the Lazanda REMS program procedures and will follow the requirements of the Lazanda REMS program.
2. I will ensure that Lazanda is only distributed to pharmacies whose enrollment has been validated in the Lazanda REMS program.
3. I will provide data to the Lazanda REMS program, including information on shipment to enrolled pharmacies.
4. I will cooperate with periodic audits or noncompliance investigations to ensure that Lazanda is distributed in accordance with the program requirements.

First Name:		**Last Name:**		**Title:**	
Authorized Signature:			**Date:**		
Distributor Name:					
Address:					
City:		**State:**		**ZIP:**	
DEA Number/Expiration Date:					
Phone Number:			**Fax Number:**		
E-mail Address:					
Preferred Channel of Communication: E-mail …☐ Fax…☐					

Please complete this form, sign, and fax it back to the Lazanda REMS program at 1-855-841-4235.

Please contact the Lazanda REMS program at 1-855-841-4234 with questions regarding this enrollment form.

This form is part of an FDA-approved REMS.

Appendix O: Lazanda REMS: An Overview for Patients and Caregivers

The Lazanda® REMS Program - An Overview for Patients & Caregivers

This overview is part of an FDA-approved REMS.

What Is Lazanda®?

Lazanda (fentanyl) nasal spray is a prescription medicine that contains the drug fentanyl. Lazanda is used to manage breakthrough pain in adults with cancer (18 years of age or older) **who are routinely taking other opioid pain medicines around the clock for cancer pain**. Lazanda can cause life threatening breathing problems which can lead to death, especially if you take more than your doctor tells you to take or if it is taken by anyone other than you.

What Is the Lazanda REMS Program and Why Is It Needed?

The Lazanda Risk Evaluation and Mitigation Strategy (REMS) program is designed to ensure the appropriate and safe use of Lazanda. The program provides specific training for doctors and pharmacists to help them select patients for whom Lazanda is appropriate. The Lazanda REMS program also helps your doctor and pharmacist provide advice and guidance to you on the correct way to use Lazanda, including how to store and dispose of Lazanda.

Lazanda can only be given to you if you are part of the Lazanda REMS program. Doctors who prescribe Lazanda, and pharmacists who give you your medication, must have been specially trained as part of the Lazanda REMS program. Information is kept on each patient who is prescribed Lazanda and for each prescription you are given. Your doctor will have talked to you about this before prescribing Lazanda for you. Your doctor will explain the Patient-Prescriber Agreement for the Lazanda REMS program which you must read and sign before receiving your prescription. After you are part of the program, you can start treatment with Lazanda.

Overview of Steps for the Lazanda REMS Program for Patients

Step 1. Joining the Program

- Your doctor will talk with you about the best way to use Lazanda, including the risks and how to store and dispose of Lazanda correctly. Your doctor will also review the Lazanda Medication Guide with you and give you a copy. Read and keep the Medication Guide.
- Your doctor may also show you a video on how to prepare, use, store, and dispose of Lazanda correctly and safely.
- Together you and your doctor will complete and sign the Lazanda REMS Patient- Prescriber Agreement.
- You will need to complete a new Patient-Prescriber Agreement every 2 years.
- Your doctor will submit a copy to the Lazanda REMS program.
- Your doctor will also give you a copy and keep a copy in your medical records.

Step 2. Getting a Prescription

- Once you have signed the Patient-Prescriber Agreement, your doctor will write you a prescription for Lazanda.
- Your doctor can help you find a participating pharmacy to have your Lazanda prescription filled, because only pharmacies that are in the Lazanda REMS program can dispense Lazanda. You can also find a participating pharmacy by calling the Lazanda REMS program at 1-855-841-4234.

Step 3. Taking Your Prescription to the Pharmacy

- The pharmacy will check to make sure that your doctor is enrolled in the Lazanda REMS program so that they are allowed to dispense Lazanda to you.
- You will be enrolled in the Lazanda REMS program when you receive your first Lazanda prescription.
- The pharmacy will remind you how to take, store, and dispose of Lazanda correctly.
- The pharmacy will also give you written information called a Medication Guide. Read and keep the Medication Guide.

Additional Program Information

For more information, you can call the Lazanda REMS program at 1-855-841-4234 or visit www.LazandaREMS.com.

Lazanda Medication Guide

[Full Medication Guide to be added]

www.LazandaREMS.com
Lazanda® is a trademark of Archimedes Development Ltd.

Bedminster, NJ 07921

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BOB A RAPPAPORT
06/30/2011